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CONTENTS

	Page
The Rockefeller Foundation	987
Taxonomy of the Yeasts. By Prof. Öjvind Winge, For.Mem.R.S.	989
British Pharmacopœia, 1953. By Prof. J. H. Gaddum, F.R.S.	990
Science in Progress. By W. L. Sumner	990
Progress in the Study of Real Crystals. By Dr. B. A. Bilby	991
The Supersonic Bang. By G. M. Lilley, R. Westley, A. H. Yates and J. R. Busing	994
Health of the School Child	996
Biosynthesis of Proteins. By Dr. P. N. Campbell and Dr. T. S. Work	997
News and Views	1002
Rockets	1006
Radioisotope Techniques in Industry	1007
Breeding-back of the Tarpan	1008
Microscopy of Plant Ashes. By Dr. J. W. Fairbairn	1008
Observations at the Royal Observatory, Greenwich	1009
United States National Academy of Sciences	1009
Kossuth Prizes in Hungary for 1953	1010
Hydration of Metal Cations. By Dr. E. Glueckauf and G. P. Kitt	1010
Potato Blight Forecasting and its Mechanization. By Dr. John Grainger	1012
X-Ray Inactivation of Polyploid *Saccharomyces*. By W. H. Lucke and A. Sarachek	1014
Letters to the Editors :	
Statistical Nature of 'Facilitation' at a Single Nerve–Muscle Junction.—Dr. J. del Castillo and Prof. B. Katz, F.R.S.	1016
Radio Echoes observed during Aurorae and Terrestrial Magnetic Storms using 35 and 74 Mc./s. Waves Simultaneously.—Prof. L. Harang and B. Landmark	1017
Fractionation of Isotopes by Distillation of some Organic Substances.—P. Baertschi, Prof. W. Kuhn and H. Kuhn	1018
Effect of Temperature on the Conductivity induced in Insulators by X-Rays.—J. F. Fowler and Dr. F. T. Farmer	1020
Degradation of Methionine by Hydrogen Peroxide.—Yoshihiko Matsuo	1021
Crystalline Trypsin.—Dr. M. Bier and Prof. F. F. Nord	1022
Mechanism of Hydrolysis of Adenosine Triphosphate catalysed by Lobster Muscle.—Edith Clarke and D. E. Koshland, jun.	1023
Possible Role of Proteolytic Enzymes in Protein Synthesis.—Robert B. Loftfield, John W. Grover and Mary L. Stephenson	1024
A Disulphide Interchange Reaction.—Dr. F. Sanger	1025
Structural Features of Antitumorigenic Corticoids.—Dr. Elvira Mardones, Dr. Rigoberto Iglesias and Prof. A. Lipschutz	1026
Multi-spots in Paper Chromatograms.—Dr. A. S. Curry	1026
The Template Theory and the Role of Transpeptidation in Protein Biosynthesis.—Dr. C. E. Dalgliesh	1027
Quantitative Estimation of the Total Solids in Fresh Whole Milk by Oxidimetry.—Arthur G. Leggatt	1028
A New Linkage in Tobacco.—Dr. B. S. Kadam and B. Radhakrishnamurthy	1028
Production of 'Three-Group Metaphases' in the Bone-Marrow of the Golden Hamster.—Dr. R. Parmentier	1029
A New Method in Staining Bacteria on Microscope Slides.—Prof. P. H. H. Gray	1030
Elimination of Inconclusive Results in the Treponemal Immobilization Test.—Hans Aage Nielsen	1030

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THE ROCKEFELLER FOUNDATION

THE Rockefeller Foundation was established in 1913; it was named after its founder, John D. Rockefeller, and although the Laura Spelman Rockefeller Memorial was combined with it in 1929, the original name was retained. Its purpose is quite simply "to promote the well-being of mankind throughout the world". An account of its activities has been prepared by Dr. Raymond B. Fosdick*, whose annual reports as president of the Foundation for more than a decade have become well known to scientific workers and others. Now he has written more particularly for the layman; he tells the story of the Foundation's achievements in the field of public health, starting with the control of hookworm, and broadening out to deal with malaria, typhus, tuberculosis and yellow fever, its contribution to medical education first in China and the United States and eventually over all the world, and the way these activities have led the Foundation to support a wide programme of medical research, and ultimately research in the social sciences and the natural sciences.

Quite apart from its value as a connected account of the development of the Rockefeller Foundation, the book could scarcely be bettered as an exposition of the contribution which science can make towards human welfare, and of the vital importance of adequate support for fundamental scientific research. These alone are sufficient reasons for welcoming the book at the present time; but there are others also why the volume is timely. The policy behind its fellowship programme of seeking solely to place the chosen Fellow in the institution where he could obtain the best possible training in the work for which he showed definite promise, no matter where the institution was located, provides a striking vindication of Mill's principle that "what the improvement of mankind and of all their works most imperatively demands is variety, not uniformity". The results of that policy refute the conception of uniformity or levelling down that finds expression, for example, in the comprehensive school. Moreover, the success of the fellowship programme, and the fruitfulness of even the limited movement of scholars across international frontiers which it has been able to foster, give plain warning of the dangers to mankind as well as to scientific advance inherent in all those tendencies which, especially during the past decade, have discouraged or prohibited scientific intercourse and the exchange of ideas.

Perhaps the main interest and chief importance of the book at the present time, at any rate, for scientific men, lie in the last two chapters. There Dr. Fosdick outlines the evolution of the principles and practices with which the Foundation now works, and finally attempts to estimate the place and significance of such a private—and voluntary—institution in the world to-day. Both chapters are as relevant to

* The Story of the Rockefeller Foundation. By Raymond B. Fosdick. Pp. 352. (London: Odhams Press, Ltd., 1952.) 25*s*. net.

problems facing us in Britain as they are to the American scene which Dr. Fosdick possibly has first in mind.

Nor is it only to the administrator of research funds, either public or private, that the first of these chapters is of interest. Next to the importance of giving the public regularly sufficient information about a private foundation, or other voluntary body, so as to secure public confidence in, and understanding of, its purposes and work, Dr. Fosdick stresses the importance of elasticity. Enlarging on this and the undesirability of the grants of a foundation being tied up to rigid and unchangeable purposes, he shows that the trustees of the Foundation, following out Mr. Rockefeller's own ideas and distrust of the dead hand, have evolved a philosophy which avoids a danger, to which Lord Beveridge directed attention in his report on voluntary action and which Lord Nathan's committee is at present considering.

Dr. Fosdick describes the provisions regarding grants which the trustees have adopted to free the future so far as possible from frozen endowments. With this healthy scepticism of the ability of one generation to foresee the needs and requirements of the next, there goes much common sense that finds expression in other principles that have not always been given proper attention in the administration of grants. "Money", wrote Mr. Rockefeller nearly fifty years ago, "is a feeble offering without the study behind it which will make its expenditure effective"; and Dr. Fosdick emphasizes the dependence of any success in the Foundation's work on careful study and investigation as a basis for judgment. Once, however, grants are made to responsible groups or institutions, no degree of control over the operation of the grants has been or should be exercised by the Foundation.

Another danger to which Dr. Fosdick directs attention is the tendency to exalt the machinery of organization above the purpose for which the organization was created. The Foundation has indeed always placed much emphasis on the need for constant self-examination and adaptability to changing conditions. Departure from this principle, in fact, threatens the ability of the voluntary body to fulfil its prime and, as Lord Beveridge pointed out, indispensable function in the world of to-day—that of providing the growing-points of society, where there is freedom to experiment in ways that would not justify the commitment of public resources, or where such resources could not be deployed with the necessary freedom. The Rockefeller Foundation has, in fact, consistently recognized that its proper objective is to prime the pump, not to act as a permanent reservoir. With rare exceptions it has sought, in undertaking a new line of work, to begin in a small way and progress by trial and error to larger ends.

Manifestly the Rockefeller Foundation has been guided by essentially the same principles as the Nuffield Foundation and the Carnegie United Kingdom Trust, though its international preoccupations have rightly led the trustees to eschew some of the more local needs and problems that the other two bodies have been able to handle without risk of frittering away reserves on the trivial. The very success of such institutions in securing officers and trustees of the requisite quality, and the vindication of their policy of seeking first and foremost the most promising and most able men—of backing talent or brains, as Wickliffe Rose put it—contrasts sharply with some of the egalitarian tendencies of to-day. The question of the future of such foundations is inevitably raised by such a contrast, and all the more because the two main conclusions which Dr. Fosdick draws from his long experience strongly support the individualist point of view. The private foundation, writes Dr. Fosdick, should be a pioneering institution rather than a regular source of support for tried and established activities; it should work on the frontiers of knowledge and experience, rather than in the more settled areas behind. Moreover, promising men and creative ideas are the fundamentals; they are far more important than money, and the best that a foundation can hope to do is to put its support in the right place at the right time. Its utmost success lies in expediting the development of ideas which, without help, might be retarded.

The experience of the Rockefeller Foundation thus fully confirms that of the Nuffield Foundation and the Carnegie Trust, and endorses Lord Beveridge's argument as to the importance of voluntary action in the world of to-day if the opportunity for blazing new trails and for pioneering and creative experiments is to continue. Inevitably the question will be asked as to whether such bodies will be able or allowed to continue to function. Dr. Fosdick notes that, in its modern sense, the Foundation is an American phenomenon of the twentieth century. Only seven such foundations were established in the United States during the nineteenth century, whereas during the first decade of the twentieth a dozen new foundations were established, some twenty-two in the second decade, and about ten a year since 1920.

Conditions in Great Britain are overweighted against the creation of any new trusts to-day, and recent reports point to the drying up of traditional sources of income. The capacity of such bodies, at least in Britain, to continue operation in the ways in which they have been accustomed in the past, and on the principles which are so strikingly endorsed by Dr. Fosdick, is already seriously endangered; if they continue at all, their choice of objectives may be less adventurous and more difficult. Considerable as are the other merits of Dr. Fosdick's book, its greatest service may well be its demonstration of the value of the contribution which the voluntary body can make to scientific advance and to social welfare in the world of to-day. It will remind us of the loss which must follow if we fail to find effective measures for ensuring that opportunities and resources remain at the disposal of the talented investigator or the creative minority to pursue their ideas untrammelled by constraint of authority, orthodoxy or topic other than their sense of duty to the community.

TAXONOMY OF THE YEASTS

The Yeasts, a Taxonomic Study

By J. Lodder and N. J. W. Kreger-van Rij. Pp. xi+713. (Amsterdam: North Holland Publishing Company, 1952.) 130*s*.

THIS book, which is a successor to Stelling-Dekker's well-known "Die Sporogenen Hefen" (1931), to Lodder's "Die Anaskosporogenen Hefen I" (1934), and to Didden and Lodder's "Die Anaskosporogenen Hefen II" (1942), is based upon such a considerable intellectual effort and such an enormous amount of experimental work that it can truly be regarded as the 'Bible' of the yeast investigator. Few groups of organisms are so difficult to arrange into a reliable system of classification as the yeasts.

The authors have attempted in a most rational manner to overcome these difficulties, and, although this has necessitated considerable rearrangements in yeast taxonomy, compelling one to become accustomed to new names for previously well-established species, there is no doubt that their efforts, in general, have been successful. The basis for this study has been a thorough investigation of the extensive yeast collection of the Centraalbureau voor Schimmelcultures in Delft.

Morphological characters are employed in the book as the basis for the primary sub-divisions, and it is obvious that such characters, which may be observed without resorting to physiological tests, are of importance and are the most convenient and practical to employ. The yeasts as a whole are first divided into two large families and one small one—the ascosporogenous yeasts (Endomycetaceæ), the anascosporogenous yeasts which produce ballistospores on sterigmata (Sporobolomycetaceæ), and yeasts which produce neither ascospores nor ballistospores (Cryptococcaceæ). The further sub-division of these families into sub-families, genera and species is based upon morphological as well as physiolcgical criteria. In all, approximately one hundred and eighty species and varieties are discussed. Whether the Sporobolomycetaceæ should actually have been included in this study is doubtful. This family, which comprises only a few species, all of which are unable to ferment, is treated in a special manner; in fact, the family name in the text does not appear as a page heading but has been replaced by "The Genera *Sporobolomyces* and *Bullera*".

It is not the place here to discuss the numerous examples of the grouping into a single species of forms which formerly were regarded as distinct species, nor to discuss the many instances of regrouping within the genera. The authors have taken cognizance of the recent investigations showing that both *Zygosaccharomyces* and *Saccharomyces* diploidize in a similar manner and are therefore nearly indistinguishable, with the result that the only difference between them is that those types originally described as *Zygosaccharomyces* often remain haploid for a longer period of time than the others. With justification, the authors have placed all species of *Zygosaccharomyces* in the genus *Saccharomyces*.

The ability of each species described to ferment a series of sugars is listed, as well as the ability to assimilate the same sugars.

In Stelling-Dekker's book it is common to encounter species described under names which the author actually did not recognize. As an example, after the description of *Saccharomyces batatæ* Saito, it is stated that this form should be correctly classified under *S. cerevisiæ*. In Lodder and Kreger-van Rij's book, on the other hand, this yeast of Saito is discussed under the name which the authors accept: *S. cerevisiæ* var. *ellipsoideus*; this is obviously an improvement over the older work.

It is correctly stated on p. 45 that "two yeast strains which show the same sugar fermentation may not be genetically alike" and that the presence in a type of one or of several genes for the fermentation of a particular sugar "must inevitably be neglected in yeast taxonomy". The authors point out that the various constant morphological differences which are found must be considered to be of greater significance in classification.

The reliability of a taxonomic character such as pellicle formation, which is partly morphological and partly physiological, may be questioned. In the description of *Pichia* and of *Saccharomyces* on p. 54 and in the generic key on p. 78, the only significant difference between these two genera is the occurrence of pellicle formation in *Pichia* and its absence in *Saccharomyces*. However, we have found (through unpublished work performed by my former collaborator, O. Laustsen) that a *Hansenula* showing typical pellicle formation was able to segregate out from a single ascus two single-spore cultures with pellicle formation and two single-spore cultures without pellicle formation. All these four cultures were haploid. This fact indicates that pellicle formation is not a completely reliable systematic character. One may also question whether the generic character of *Hansenula* of nitrate assimilation is sufficiently important, in view of the fact that in many of the anascosporogenous yeasts both nitrate assimilating (N+) and non-nitrate assimilating (N−) species are found in the same genus.

It must be admitted that the difficulties encountered in erecting an acceptable system of yeast classification may justify the use of criteria which the systematist finds practical, even to the exclusion of a natural relationship and even if such a classification is not always completely logical. Of prime importance is whether the species can be identified by the system proposed, and in this respect the present work is certainly to be preferred to the earlier attempts.

It is inevitable that in such an extensive work errors will occur. With regard to minor errors, it can be noted that, on p. 333 as well as on other pages, "*Lypomyces*" is used instead of *Lipomyces*. In this connexion, it should be mentioned that, in the transfer of *Torula lipofera* to the genus *Lipomyces* (p. 335), the species should be called *Lipomyces lipofer* (not *lipoferus*, which is incorrect Latin). In the species index on p. 712 one finds "*Zygopichia*" as a heading for a long list of species. This should read "*Zygosaccharomyces*". It is incorrect to say that Lindegren (1949) "supposes that a dominant gene controls a high rate of enzyme production, whereas its recessive allele only is able to produce a very small amount of enzyme" (p. 46). This is the view held by Dr. Roberts and myself, proposed in 1948 in connexion with galactozymase, while Lindegren maintains that the recessive type, through mutation, may acquire the ability to synthesize the enzyme.

I am not in complete agreement with the statement that "If giant colonies are to be made the yeast is inoculated on malt gelatin in Petri dishes or Lindner flasks and observed after 4–8 weeks' incubation at 21° C.". I find that a lower temperature (15° C.)

produces a more characteristic surface appearance of the colonies, and that an incubation time of 3–4 weeks is quite sufficient. The authors have employed Einhorn tubes for their routine qualitative fermentation tests, although they consider Durham tubes more satisfactory. Actually, whether Einhorn or Durham tube is to be preferred depends upon the construction of the Einhorn. However, both tubes suffer the defect of allowing the carbon dioxide produced during fermentation to diffuse out of the sugar solution; this can, however, be overcome by employing mercury in the Einhorn. In our laboratory, we prefer the small Winge fermentometer, which is easy to use and inexpensive and which completely prevents gaseous diffusion.

These critical comments should, however, not detract from the merits of this imposing work, and there is good reason for congratulating the authors upon its completion. The book is provided with drawings which are a considerable improvement over those appearing in the earlier systematic works mentioned above. Nineteen new species and varieties have been erected and are described in Latin.

Øjvind Winge

BRITISH PHARMACOPŒIA, 1953

British Pharmacopœia 1953

Published under the direction of the General Medical Council. Official from 1 September 1953. Pp. xxiv+894. (London: Pharmaceutical Press, 1952.) 50*s*. net.

THE eighth "British Pharmacopœia", which becomes official on September 1, 1953, follows its predecessor after an interval of only five years. The Pharmacopœia Commission is to be congratulated on this acceleration of its output, which cuts down the time for this important standard work to get out of date. Much has happened during the past five years and many new drugs now appear for the first time, including aureomycin, cyanocobalamin, decamethonium, dibutylphthalate, ethyl*bis*coumacetate, folic acid, methadone, sodium aminosalicylate, troxidone and fifty-four other substances or preparations. There are also fifty-two new monographs which appeared in the addendum published in 1951 and now appear for the first time in the "Pharmacopœia" itself. The preparation of so much new matter is itself a formidable task; but the Commission has done much more than this. The number of old monographs ejected is even greater than the number of new monographs admitted. The Commission has shut its mind against sentiment and thrown out such old favourites as grey powder, Blaud's pill, squill, iodoform and aromatic spirit of ammonia. Some drugs, such as amidopyrin and diamorphine and sulphonal, are now thought too dangerous for general use, though some doctors still believe in them. Certain drugs of comparatively recent origin, such as acriflavine and dicoumarol and thiouracil, have been replaced by better drugs in the same class. The only remaining lozenge contains nothing but penicillin and sugar. As these examples will show, the Commission has spared no effort to ensure that the new book shall be efficient rather than picturesque and shall contain all essential drugs and nothing more.

The form of the book is more attractive than ever before. Latin has been deposed from pride of place, and the main title of each drug is given in English. The alphabetical arrangement has been improved, so that tincture of digitalis comes close to digitalis instead of being segregated with the other tinctures. Doses are given in the metric system, and the other weights and measures still used by old-fashioned doctors sometimes appear in brackets.

There is an interesting innovation in Appendix 15. Biological assays were first officially discussed in the 1932 "Pharmacopœia", and since then new methods of assay have been introduced from time to time, with various different recommendations for the design of the experiment. Some of the older ones were rather crude, and some of the newer ones were rather difficult to understand without much mathematical training. All such assays are based on the same general principles, and the Commission has prepared a section dealing with the design and accuracy of biological assays in general. It has thus been possible to eliminate repetition in the description of the separate assays and to introduce a simplified method of calculation which gives results accurate enough for all practical purposes. The methods now recommended are described in about a dozen pages with six examples of actual calculations, a table of t, a table of probits and a table of weights for probits. These methods of calculation do not include all the refinements recommended by some authorities, but they also do not include the inaccurate and unsatisfactory approximations recommended by other authorities; thus they should be found satisfactory for routine assays.

The new "Pharmacopœia", like all its predecessors, represents a great advance; but in this case the advance has been achieved in a very short time.

J. H. Gaddum

SCIENCE IN PROGRESS

Science in Progress

By Bradley M. Patten, George W. Corner, Arnold Gesell, H. J. Muller, T. M. Sonneborn, Ralph W. G. Wyckoff, Carl D. Anderson, Farrington Daniels, J. R. Dunning, Emil Artin, George Gaylord Simpson, Raymond M. Fuoss. Edited by George A. Baitsell. Seventh Series. Pp. xvii+512. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1951.) 40*s*. net.

THIS beautifully produced book is a worthy successor to the six former volumes in the series. Recent major contributions to many fields of science are described by the men who have been partly or wholly responsible for them. The new volume includes articles by two Nobel prize-winners and eight members of the United States National Academy of Sciences.

Dr. Bradley M. Patten writes of his research on the first heart-beats and the beginning of embryonic circulation in the developing chick; then follows a study of the action of ovarian hormones in the Rhesus monkey by Dr. George W. Corner, director of the Department of Embryology at the Carnegie Institution of Washington.

Dr. Arnold Gesell, who is known throughout the world for his work on the psychology of young children, presents a well-illustrated account of the psycho-physical development of the infant; analysis of cinema photographs of the child's reaction to its environment has been made possible by the use of a photographic dome for recording infant behaviour patterns. Then follows a long section by Dr. H. J. Muller, of Indiana University, on radiation damage

to the genetic material, in which much more research is called for on the long-term effects on tissue produced by frequent small doses of X-rays and other forms of radiation usually assumed to be safe.

The author of the next chapter, Prof. Tracy M. Sonneborn, professor of zoology in Indiana University, discovered a mating reaction associated with the conjugation of *Paramecium*, which culminated in the establishment of the concept of the plasmagene in cytoplasm, and he writes that "The ultimate task will be to reunite the nuclear and cytoplasmic components of the genetic system in an integrated, interreactional conception of the genetic system of the cell and the study of the function of each in the work of the whole". Dr. R. W. G. Wyckoff has a chapter on the structure of crystals, and his work is illustrated with some remarkable electron-microphotographs of virus crystals, in which the actual molecules may be seen. Carl D. Anderson, the discoverer of the positron, sums up the present position with regard to our knowledge of the elementary particles of physics, and Farrington Daniels, of the University of Wisconsin, reviews the possibilities of the future use of atomic and solar energy; no less than fifty fields of research in the utilization of the sun's energy are listed.

Pure mathematics has been given consideration in a section by Emil Artin, of Princeton University, in which the theory of braids is worked out by combining topology and the theory of groups. Finally, there are important chapters on the fauna of Latin America by George Gaylord Simpson, and on the physical chemistry of polymers by Raymond M. Fuoss. Each chapter is well documented.

W. L. SUMNER

PROGRESS IN THE STUDY OF REAL CRYSTALS

Institut International de Physique Solvay
Neuvième Conseil de Physique tenu à l'Université Libre de Bruxelles du 25 au 29 septembre 1951. L'État solide: Rapports et discussions. Pp. 577. (Bruxelles: R. Stoops, 1952.) 650 francs.

THE scientific committee of the Institut International de Physique Solvay convenes periodically a conference at which problems of some branch of physics are reviewed. The reader learns from the table of contents or from an aside on p. 167 that the main theme of this conference report on the solid state is that of imperfections and transformations, and principally the former. The book is a collection of papers, with discussions, and the majority deal specifically with studies of metals, although most problems treated have a wider application. Some of the papers review an aspect generally, but most describe particular developments with which the authors have been personally associated. Much of the subject-matter has, of course, been published already, and indeed, as is perhaps inevitable in a field in which such rapid developments are occurring, has also been discussed at recent conferences of similar scope. There is, however, some new work of interest to the specialist, and although its nature makes it rather disjointed, the book is to be recommended to a wider circle as an authoritative account of the state of development at September 1951 of the topics discussed.

The book begins with a fascinating paper by C. S. Smith describing the recent work on grain boundaries which has been stimulated by comparing the polycrystalline solid with a soap froth. There are three other papers concerned directly with grain boundaries and their properties. W. G. Burgers, discussing recrystallization, gives a comprehensive review of new data and ideas which have appeared since 1940 and includes a survey of new techniques for studying structural changes. G. W. Rathenau describes the application of one of these—electron emission microscopy—to the direct study of grain-boundary migration in metals at high temperatures. Calculations on the energy of grain boundaries using the dislocation model are reported by W. Shockley.

There are five papers about transformations. E. Rudberg reviews recent Swedish work, and this is supplemented later by a brief note from G. Borelius. Age-hardening and the order–disorder transformation are treated by W. Köster and A. Guinier, while C. Crussard describes his theory of the interference of thermal waves and its applications. Lattice vibrations are also discussed in J. Laval's detailed account of his theoretical work on the elastic properties of a perfect crystal in which the interatomic forces are not central.

The remaining papers are all concerned directly with the theory of dislocations. E. Orowan discusses the dynamics of slip and examines critically some of the fundamental hypotheses of this theory. There are articles by F. C. Frank on crystal growth, F. Seitz on the generation of vacancies by moving dislocations, and A. H. Cottrell on the yield-point in iron. N. F. Mott discusses current ideas on work-hardening, recovery and creep, and there is a short note from U. Dehlinger.

The dislocation theory has made great strides since the Second World War. At the time of the Bristol Conference in 1947, perhaps the most convincing parts of the theory were the explanations it afforded of the influence of traces of impurity on mechanical properties (atmosphere theory), and of the phenomenon of polygonization. Since that time the observation of spiral steps on the surfaces of growing crystals has provided direct evidence for the existence of dislocations. Also, the actual propagation of slip lines across the surface of a specimen has been studied with the high-speed camera. At the same time, it is now possible to understand how slow-moving dislocations can multiply. Already, important new evidence of the co-operative movement of dislocation arrays, predicted and referred to briefly in the paper of W. Shockley at this conference, is available in the experiments of Washburn and Parker, while the comparison of absolute grain-boundary energies for small angular disorientations with the predictions of the dislocation theory appears to make possible the first quantitative test of this theory. Much of the theory remains, however, frankly speculative, and, as E. Orowan emphasizes, the need for experimental support for its foundations is acute. There is some ground for confidence, however, that this will be increasingly forthcoming in the near future.

Despite its title, English-speaking readers will be glad to know that some three-quarters of the book is in their language. It is perhaps unkind to comment on the numerous errors of editing which result; but it is impossible to refrain from quoting the apposite heading of "Creed and Polygonisation".

B. A. BILBY

Classical Mechanics

By Dr. D. E. Rutherford. (University Mathematical Texts.) Pp. viii+200. (Edinburgh and London: Oliver and Boyd, Ltd.; New York: Interscience Publishers, Inc., 1951.) 10*s*. 6*d*. net.

DR. D. E. RUTHERFORD'S aim is to provide a concise and unified account of classical theoretical mechanics from the beginning up to Hamilton's principle. There are five chapters, dealing respectively with kinematics, the nature of force, dynamics of a particle, dynamics of rigid bodies and generalized co-ordinates. A surprisingly large amount of information has been packed into a small space. For example, Chapter 4 contains not only the usual elementary theorems on rigid dynamics, and an account of Euler's equations and the top, but also some statics, including centre of gravity, Poinsot's central axis and virtual work. Chapter 5 includes Lagrange's equations, normal modes of oscillation, stability, Hamilton's equations and Hamilton's principle. There are examples for solution at the end of each chapter, the total number being 108, and an index.

There can be no doubt as to the value of the matter contained in the book; but it is rather puzzling to know for what type of student it is intended. The introduction points out that a knowledge of calculus, co-ordinate geometry, and vectors is required. It does not mention that p. 141 uses the notation and two theorems of matrix theory. Also there is no statement as to the previous knowledge of dynamics required; but it is obvious that a beginner will find great difficulty with some of the early pages—for example, p. 13 on moving axes. The introduction stresses that the book is arranged in logical order and not in order of increasing difficulty, and that "many readers may find it advisable, therefore, to read the various sections in an order other than that in which they are presented. Teachers will, no doubt, advise their students on this point according to the students' maturity". This last sentence transfers the task of presenting the subject in a form that can be easily assimilated from the author's to other shoulders.

H. T. H. Piaggio

The Cold Working of Non-Ferrous Metals and Alloys

A Symposium on Metallurgical Aspects of the subject held in London on the occasion of the Annual General Meeting of the Institute, 14 March 1951. (Institute of Metals Monograph and Report Series, No. 12.) Pp. 207. (London: Institute of Metals, 1952.) 15*s*.

THE five papers which make up this symposium are reviews of particular aspects of cold-working, such as wire-drawing, cold-rolling and pressing. The practical techniques employed are examined in relation to the optimum process conditions for the more commonly used non-ferrous metals and alloys, with the fundamental aspects of cold-working reviewed in one general introductory paper. This may represent a just proportion in a work on applied metallurgy, but even in this paper the discussion is not extended to cover any detailed theory. The interpretation of cold-working phenomena in terms of dislocations, and the treatment given of deformation textures, are both so generalized that they give no more than a brief indication of current ideas. This is unavoidable in the space of the few pages devoted to these subjects, and the selection of the material, which must have been a difficult task, is, on the whole, well judged. The volume is clearly a most useful work for those actively connected with industrial processes which involve cold-working in any form. Most problems are touched upon, and where detail is inadequate the quoted references may be followed up. However, as the development and extension of such techniques depend upon a fuller understanding of the metallurgy and physics of the deformation mechanisms, a closer consideration of fundamentals would have widened its appeal.

A. J. Kennedy

Entwicklungsphysiologie

Von L. v. Ubisch. Pp. 85+16 plates. (Berlin: F. W. Peters, 1952.) n.p.

PROF. VON UBISCH has made important contributions to the experimental embryology of a wide variety of forms—echinoderms, ascidians, *Ascaris* and amphibians among them. He has, however, stood somewhat outside the major schools, such as the German, the Swedish and the Belgian, which have tended to dominate the subject in the past few decades, and his contributions have perhaps received rather less attention than was their due. It is therefore all the more gratifying to have from his pen a general treatment of the field. His little book is exceedingly short and is aimed at a student audience. Its brevity has enforced a most admirable clarity of theoretical outlook. Von Ubisch presents a very modern point of view: that the essential basis of differentiation is to be sought in the interaction between nuclei and locally differentiated cytoplasms, by which different sets of genes become activated or inhibited. In the space at his disposal the author can do little more than adumbrate this proposition and has had to forgo a discussion of much of the widely diversified evidence which bears on it, particularly from the side of genetics. However, little of major importance is omitted from his summary of the facts of experimental embryology, and his book is probably the best short and up-to-date account of it.

C. H. Waddington

Leibniz und das Reich der Gnade

Von Kurt Hildebrandt. Pp. viii+505. (Haag: Martinus Nijhoff, 1953.) 26.50 guilders.

CONTEMPORARY scholarship may perhaps be said to have 're-discovered' Leibniz; the stately volume here under review is not the only evidence of this trend in recent months, but it is a contribution of a somewhat special character, designed to set the great thinker at the centre of a specifically European philosophy, occidental in spirit and intended to be "understanded of the people". To this extent, it represents a return to the early Greek concept, when the love of wisdom was taught not so much as an academic subject, as a life to be lived. Thus, a not inappropriate rendering of the title of the present work might be "Leibniz and the Realm of Grace".

The first part is largely biographical, including the encounters with Locke and Newton. Next follows a typical *Systematik*, an assessment of the creative faculty in mankind, and the problem of good and evil. (The celebrated "Theodicy" comes in for attention earlier.) Finally, there is the inevitable discussion of action and re-action, including questions of belief and configuration. The latter should not be confused with the *Gestalt* of to-day; for Leibniz, 'shape' was more of an abstraction than it is to us. The book—a work of real distinction—concludes with a useful chronological table.

F. I. G. Rawlins

An Explaining and Pronouncing Dictionary of Scientific and Technical Words

10,000 Scientific and Technical Words in 50 Subjects explained as to a Person who has little or no Knowledge of the particular Subject. By Dr. W. E. Flood and Dr. Michael West. Pp. viii+397. (London, New York and Toronto: Longmans, Green and Co., Ltd., 1952.) 12*s.* 6*d.* net.

THIS is a very useful compact dictionary, and it will have a wide acceptance. In less than four hundred pages, ten thousand scientific and technical words in fifty subjects ranging from architecture to zoology are explained and given correct pronunciations. Like Larousse and Nuttall before them, but in a more generous and enlightened manner, the authors have supplied thirteen hundred pictures and diagrams to assist them in their explanations. A simple and effective method of cross-reference has been used in the book, and thus its value has been enhanced. The authors set themselves a number of working rules when they made their dictionary, and, by following these, their work has not degenerated into an unsatisfactory encyclopædia. Only a captious critic would find details which would evoke comment.

Why has oxygen not been given when nitrogen and hydrogen have? Why axolotl and not salamander, geriatrics and rheology but not cybernetics, harmonic but not consonance or temperament in their acoustic sense, coma with two meanings but without reference to lens aberrations? There is tawny port wine (which is important), but not polyploid, serology or the biological use of the word spindle. Very few of the explanations have suffered through the process of condensation, but some seem to need qualification; for example, "calciferol is found in yeast", "burn bones to make lime". There is a table which gives British and metric weights, measurements and temperatures, but atomic weights are not usually given. The most hypercritical reviewer would have to admit that in such a small but comprehensive volume some matters of choice must be left with the authors.

The book is excellent value for money and is attractively produced. It will be handy as a reference work for all intelligent citizens, even if their primary interest is not science. Many will be tempted to browse in it. W. L. SUMNER

Tables of the Bessel Functions of the First Kind of Orders Seventy-nine through One Hundred and Thirty-five

By the Staff of the Computation Laboratory. (Annals of the Computation Laboratory of Harvard University, Vol. 14.) Pp. x+614. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1951.) 52*s.* net.

THE publication of this volume completes a project inaugurated in 1944 by the Computation Laboratory of Harvard University and continued since, at intervals, whenever the Laboratory's automatic computer was not engaged on work of higher priority. The results are given in a series of large volumes, of which this is the twelfth. Previous volumes in the series have been reviewed (*Nature*, **160**, 772 (1947) and **163**, 152 (1949)), and there is not much to add to what has already been said.

The original project was to tabulate the function $J_n(x)$, for positive integer n up to 100 and for values of x up to 100, to ten decimals, except that, for $n = 0(1)3$, values are given to eighteen decimals. For x greater than 25, the tabular interval has so far been 0·01, but in the present volume it is increased to 0·05 at $n = 97$, and again to 0·1 at $n = 112$. It has been found possible to increase the range of n up to 135, beyond which $J_n(x)$ is not significant to the tenth decimal at $x = 100$. The range of x has been closed by the inclusion of a ten-decimal table of $J_n(100)$ up to $n = 135$, and a table of $J_n(n)$ for $n = 1(1)100$ is also given.

Dr. H. Aiken and his staff—and also the machine—are to be congratulated upon the completion of the great task which they set themselves, and the result is probably the most extensive piece of tabulation which has so far been attempted and brought to a successful conclusion. W. G. BICKLEY

Du Pont

The Autobiography of an American Enterprise. The Story of E. I. Du Pont de Nemours and Company published in commemoration of the 150th Anniversary of the Founding of the Company on July 19, 1802. Pp. vi+138. (New York: Charles Scribner's Sons, 1952.) n.p.

THIS handsome volume, richly illustrated partly in colour, traces the development of a famous American firm from its foundation in 1802 near Wilmington, Delaware, by a young refugee from France, Eleuthère Irénée du Pont, who had been a pupil of Lavoisier. Many of the illustrations connected with the early period are taken from the contemporary press and are of great interest in respect of such things as costume. The illustrations showing present-day conditions may seem at first sight too familiar to warrant inclusion; but in due time they also will come to be records of past days, equally interesting and valuable. The volume, which has drawn upon many sources, including the records of the firm, is one of the most interesting and attractive of its type which has come to the notice of the reviewer, and any library which looks to the future should make a point of including it.

The Bay

By Gilbert C. Klingel. Pp. x+278. (London: Victor Gollancz, Ltd., 1952.) 12*s.* 6*d.* net.

THE bay of which Gilbert Klingel writes is the Chesapeake, stretching to the east of Maryland and Virginia, and so called after the American Indians who first peopled its shores. The coast is deeply indented with wide river mouths, long lagoons, estuaries, and thousands of small creeks, so that, it has been said, if the shore-line were straightened out it would stretch more than four thousand miles. For twenty years Klingel has watched the bay with the acute perceptions of an enthusiastic and experienced naturalist. In this book he describes the bay in many moods as well as the remarkable variety of its living forms. The latter he has studied above, on and below the surface of the bay; possibly his best descriptions are those of the living creatures which he met underwater. For Klingel is an experienced underwater observer and, whether in helmet, diving-suit or his curious home-made 'Bentharium', his close contacts with submarine life have produced descriptions of animal behaviour which put him in the top flight of writers on natural history. One of the best chapters is an account of happenings during a whole twenty-four hours spent in the heart of a swamp. The chapter on luminescence is equally good, while the author's description of his experience with the 'Bentharium' is one of exciting adventure.

THE SUPERSONIC BANG

By G. M. LILLEY, R. WESTLEY, A. H. YATES and J. R. BUSING
Department of Aerodynamics, College of Aeronautics, Cranfield, Bucks

THE reason for the bang or bangs heard by ground observers after an aircraft has exceeded the speed of sound has been the subject of much speculation. In previous communications, Gold[1], Warren[2] and Rothwell[3] have based their explanations on Huygens's wavelet construction for a moving source which replaces the aircraft. They have shown that an observer will experience a bang if $-\mathrm{d}r/\mathrm{d}t = c$, where r is the (scalar) distance between aircraft and observer, and c is the speed of sound. This is simply the condition for the pulse waves emanating from successive elements of the supersonic flight path to form an envelope or wave front (Mach wave).

For a source moving in a straight line at a speed which increases and then decreases through the speed of sound, two curved wave fronts are formed, joined at their outer extremity by cusps (see Figs. 1–4 inclusive).

In the simple theory it is assumed that these waves, which eventually move ahead of the retarded source, cause bangs as they pass the observer. Although the calculated time interval between the two bangs, and the strength of the first wave front, have shown reasonable agreement with measured values obtained from a restricted series of flight experiments, the calculations to date do not predict a second wave front of comparable strength to the first. Experiments with aircraft in dives have shown, however, that the strength of each component of the double-bang is approximately equal. If instead of the Mach wave configuration the shock waves around an aircraft, in unsteady as well as steady flight, are considered, this discrepancy between theory and experiment does not arise.

Since it is only necessary to discuss the pattern of the shock wave at large distances from the aircraft, it is possible to replace the aircraft by an equivalent body of revolution. This avoids the complicated

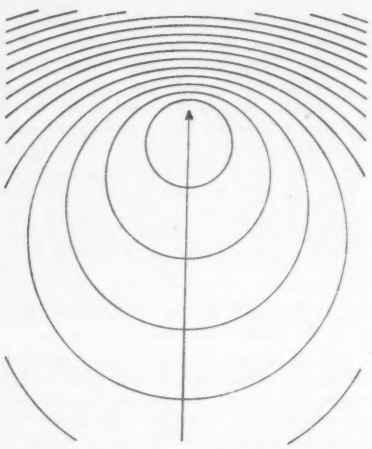

Fig. 1. Source moving along a straight line with constant subsonic speed, $M = 0{\cdot}8$

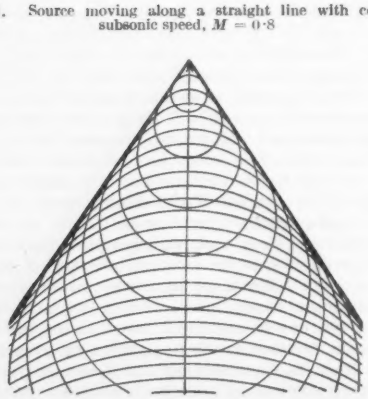

Fig. 2. Source moving along a straight line with constant supersonic speed, $M = 1{\cdot}6$

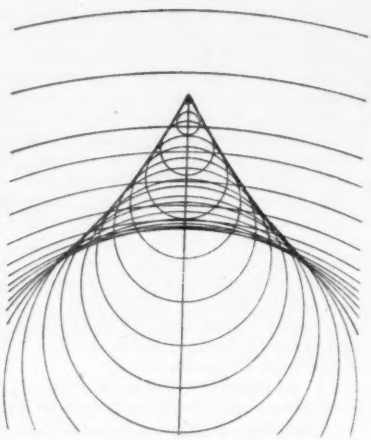

Fig. 3. Source accelerating along a straight line from subsonic to supersonic speed

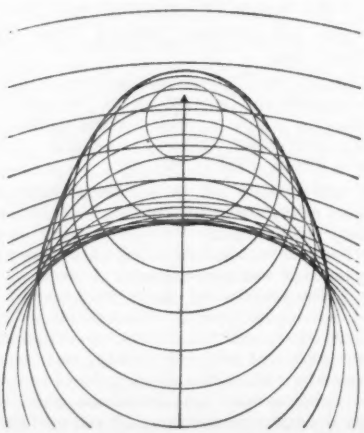

Fig. 4. Source accelerating along a straight line from subsonic to supersonic speed and then retarding to subsonic speed

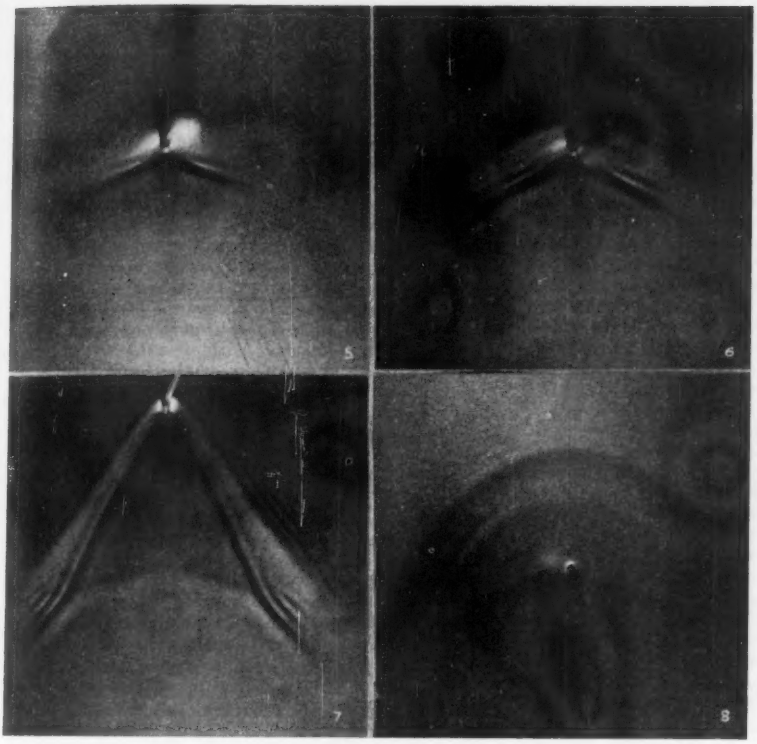

Fig. 5. Aerofoil accelerating (subsonic Mach No. $\sim 0{\cdot}95$)
Fig. 6. Aerofoil accelerating (supersonic Mach No. $\sim 1{\cdot}1$)
Fig. 7. Aerofoil at maximum speed (supersonic Mach. No. $\approx 1{\cdot}8$)
Fig. 8. Aerofoil retarding (subsonic Mach No. $\sim 0{\cdot}6$)

treatment of the multi-shock interaction close to the aircraft. Simple experiments[4] based on the hydraulic analogy technique, using towed models, have verified the shock-wave explanation of supersonic bangs (see Figs. 5–8).

Shock-wave Configuration in Unsteady Flight

When a body is uniformly accelerated from rest up to high subsonic speeds below the critical Mach number (the Mach number of the body at which the local speed near the surface first reaches sonic speed), the flow pattern around the body at each instant will not be markedly different from that at the corresponding steady speed. At flight speeds above the critical Mach number, shock waves are formed around the body at the end of the local supersonic region. These shock waves move back towards the tail as the Mach number of the body is increased. At a sufficiently high subsonic Mach number, the tail shock becomes bifurcated with its rear member nearly normal to the wake (Fig. 5).

When the acceleration of the body is continued to supersonic speeds, a bow wave is formed just ahead of the body (Fig. 6). Unlike the front tail wave, it remains approximately normal, near the body, at least over a finite range of supersonic speeds. It becomes attached to the nose, if sharp, above a certain supersonic Mach number, which is a function of the nose angle (Fig. 7). The extent of the bow wave and its distance from the nose is a function of the body geometry, the body speed and acceleration, as well as the complete time-history of the motion. Thus the bow wave can only attain its steady state configuration after an infinite time. Away from the body axis the interaction of the expansion waves (which are necessary to accelerate the flow between the bow and tail waves) with the bow wave reduces its inclination relative to the flight path. It can be seen, therefore, that marked differences occur between the formation of the bow and tail waves. In the latter case, the wave is concave forwards, close to the body (Fig. 5), and the formation of its rear member is therefore analogous to that of the Mach waves associated with an accelerated point source (Fig. 3). The bow wave is, however, convex forwards (Fig. 6), and a simple qualitative analysis will show that the flow inhibits the formation of cusps at its outer extremity. Thus for a body accelerated from subsonic to supersonic speeds, the shock formation consists of a bow wave ahead of, or attached to, the nose, and separated from the front tail wave by a system of expansion waves, plus a rear transverse wave joined to the front tail wave at its outer extremity.

When the body is retarded and its speed falls below the critical Mach number, the bow wave will have travelled far ahead of the nose, since it detaches itself from the body when its speed is just above sonic. The front tail wave will travel slowly towards the nose, and in doing so becomes approximately normal to the surface. Its shape changes and it becomes convex to the direction of the motion. It moves ahead of the body when the speed of the latter falls below the critical Mach number. The rear tail wave moves towards the body, overtakes it, and finally it also moves ahead of the body (Fig. 8). Thus the shock wave formation ahead of a body, retarded from supersonic motion of finite duration to subsonic, is a bow wave separated from the front tail wave by a system of expansion waves, and trailing farther behind a rear transverse wave joined to the front tail wave at its outer extremity. The two members of the tail wave tend to coalesce after a finite time. Thus at a large distance ahead of a body executing this simple manœuvre, we shall have either two or three shock waves each travelling at approximately the speed of sound. The first two waves will have similar strengths, whereas the third wave, if it has not overtaken the front tail wave, will be considerably weaker.

The distance apart of the shock waves can be calculated approximately as follows. The distance between the bow and the front tail wave is equal to the speed of sound multiplied by the time for the body to slow down from sonic speed to just below its critical Mach number. The distance between the bow wave and the rear tail wave depends on the time-history of the accelerated and then retarded motion of the body. When this is known, the calculation can be completed, since it has been shown that the rear tail wave is left behind in the wake of the body at the commencement of the supersonic motion, while the bow wave separates from the body at the conclusion of the supersonic motion. In addition, as a first approximation, it may be assumed that the free shock waves are moving normal to themselves at the speed of sound. The spread of the shock waves after a given time can be found approximately from the corresponding Huygens wave diagrams for the motion of a point source which replaces the body.

In the case of steady motion at supersonic speeds, the bow and tail shock waves are of infinite extent, except where they are reflected from solid surfaces. The rear tail wave is now infinitely far behind the body and hence is not observed.

Noise from High-speed Aircraft

In the case of jet-propelled aircraft travelling at high subsonic speeds, the main noise is due to the turbulent motion created by the jet. At supersonic body speeds, the sensation of noise caused by shock waves, even when they are weak, is very much greater than that due to other sources, although the duration of the noise is very short. For a body flying at constant supersonic speed at a fixed altitude, the bow and tail shock waves will sweep over the ground, and these and their reflexions will be heard by observers as separate bangs, only if their time interval is greater than about 0·02 sec. For a body executing a high-speed dive, during which the speed increases and then decreases through sonic speed, ground observers may hear one, two or three bangs depending upon their location and the time-history of the motion. In the cases where more complicated manœuvres are executed, simple analysis will determine the number of bangs to be expected.

In the discussion above, the refraction of the shock waves through a non-uniform atmosphere has not been considered. This will not invalidate the above results; but it should be noted that for certain manœuvres the shock waves produced around the body at altitude will not penetrate to the ground.

[1] Gold, T., *Nature*, **170**, 808 (1952).
[2] Warren, C. H. E., *Nature*, **171**, 215 (1953).
[3] Rothwell, P., *Nature*, **171**, 216 (1953).
[4] Lilley, G. M., and others, College of Aeronautics Report 71 (1953).

HEALTH OF THE SCHOOL CHILD*

THE report of the Chief Medical Officer of the Ministry of Education for the years 1950 and 1951 shows that the mortality-rate of children aged 5–14 years is still falling. Of the 3,341 children who died in 1950, 851 met their deaths through accidents—about half of them motor accidents. 294 children died of tuberculosis compared with 937 in 1938, 207 of cancer and 153 of poliomyelitis. Deaths from diphtheria continued to fall: 16 children died in 1950 compared with 1,733 in 1938. The general health of the children continues to improve.

There has been a remarkable reduction in skin disease among children. During 1947–51 the number of children with scabies, impetigo and ringworm of scalp has fallen from 108,000 to 34,000. Acute rheumatism is being reduced, and although more than 4,000 children a year suffer from this disease, this is less than a third of the number ten years ago.

Cleanliness of school children is also improving. "Even so," states the report, "it is inexcusable that 347,544 children (6%) were found verminous in 1951. Parents of consistently verminous children must have very little self-respect." A persistent campaign is being waged against this problem; but success in preventing repeated re-infestation depends upon the measures taken to deal with possible verminous conditions in other members of the family—in particular, the pre-school child and the young adult. In one area, methods of treatment include an offer of DDT hair-cream to the parent.

Nearly 4½ million children were examined or re-examined during 1951 by school medical officers. 157,566 children were found to have defects in vision and a further 37,499 children required treatment for squint compared with 31,189 in 1949. Nearly three children in every thousand required treatment for defective hearing, and nearly five in every thousand were recommended to be kept under observation. More attention is now being paid to the ascertainment of deafness in children as it is considered vital to treat them early in school-life.

The report includes a highly critical survey of open-air schools by four medical officers of the Ministry. In their account of premises they state: "There are in this country some first class open-air schools which have been designed to give the children full benefit from fresh air and sunlight, but there are others which are merely ramshackle wooden huts, unpleasant to live in and ugly to look at. In some of the schools the walls were simply screens, made partly of wood and partly of canvas extending from the floor about 2–4 feet from the ceiling. The rooms were without any means of heating and were often without artificial light. In wet, windy weather, rain drove in between and above the curtains so that the floor and furniture were often wet. We saw children scraping frozen snow off the desks and chairs before they could be used. In cold weather the children sat at their desks wearing hats, caps, coats, scarves and gloves, and with blankets round their legs. As doctors, we cannot feel that refrigeration or dampness contributes to health and, therefore, we strongly condemn the 'bandstand' type of classroom. In one school on a wet day we saw the children lying on damp canvas stretchers in an unheated, open-fronted stone-floored shed, with the rain driving in at the front and leaking through the roof".

The report explains that a well-conducted open-air school is of great value for delicate children, and apart from its physical benefits, they usually find sheer pleasure in being out of doors; but they must be kept dry and reasonably warm. There is still a place for these schools, especially in industrial areas; but no expansion of existing provision is considered necessary. "With a rising standard of living, better housing, the provision of meals and milk in schools, and with a fuller appreciation in the ordinary schools of the varying needs of individual children, it may be that the need for special schools for 'delicate' children will diminish with the years."

* Health of the School Child. (H.M.S.O.) 5s. net.

BIOSYNTHESIS OF PROTEINS*

By Dr. P. N. CAMPBELL and Dr. T. S. WORK
National Institute for Medical Research, Mill Hill, London, N.W.7

BIOCHEMICAL research has been concentrated until recently on the degradative rather than on the synthetic reactions of the living cell. This was the natural outcome of limitations imposed by technique. The products of degradation are small molecules amenable to investigation by the classical techniques of organic chemistry, whereas the products of synthesis are often of high molecular weight and of embarrassing complexity. The introduction of isotopic tracers, of chromatography and of high-speed centrifuges has made possible a reorientation of research. Among the many problems open to attack by these new methods, that of protein synthesis is among the most formidable and most important.

Proteins such as those of hair and skin cannot be said to have any definite molecular weight and they may well have no definite molecular structure, but the smaller water-soluble proteins when purified show many of the attributes of homogeneous molecular species. Thus, for example, it seems likely that all the insulin molecules produced by one animal are of identical structure. There is no indubitable proof of this view, but the recent determinations by Sanger and Porter[1] of protein end-groups, the work of Porter[2] and of Schroeder[3] on amino-acid sequences adjacent to the end-groups, and especially the recent work of Sanger[4] on the amino-acid sequences in insulin, all suggest that a single purified protein is a single molecular species.

It is known from the classical investigations of Nuttall[5] and others that the morphological differences between species are no more distinct than the serological differences between the proteins of those species. Thus, for example, purified duck ovalbumin can be distinguished from purified hen ovalbumin by immunological methods[6]. In the same way the serum globulins, the fibrinogens, the trypsins and the hæmoglobins of two closely related species may be indistinguishable by physical methods but serologically distinct. The work of Landsteiner[7] and others has suggested that immunological specificity is the reflexion of a specific chemical structure. Thus it is reasonable to suppose that each type of cell possesses enzymic mechanisms capable of exact control of the amino-acid composition and sequence of all its proteins. This conclusion is fortified by the recent investigations of Sanger[8], of Lens[9] and of Craig[10] on sheep, pig and bovine insulins. These proteins are indistinguishable by physical methods and are of equal biological potency but are chemically distinct. Apparently the pancreatic cells of each species control the exact reproduction of a complex polypeptide pattern characteristic of the species. For some proteins the specificity of structure appears to be controlled within even narrower limits than that of the species and is characteristic of the family, the specific immunological character of the protein then being inherited within the family. To understand the mechanism of protein synthesis is thus a step towards understanding the inheritance of character and the continuity of the species.

* Based on two lectures given by Dr. T. S. Work, honorary lecturer in pharmacology, at University College, London, on February 16 and 20.

Protein Turnover in the Adult Animal

In the early years of the present century much progress was made in the study of protein digestion. By 1920 it was generally accepted that ingested protein was degraded by proteolytic enzymes in the stomach and gut and that the nitrogen was absorbed as free amino-acids[11]. The work of Folin[12] indicated that in the adult the dietary amino-acids were rapidly oxidized, and thus most of the nitrogen was excreted as urea. It was assumed, therefore, that protein synthesis almost stopped when growth stopped. However, in 1935 Borsook and Keighley[13] presented evidence to suggest that there is a continuous and high rate of protein synthesis even in the adult animal. In 1939 this conclusion was supported by the results of Schoenheimer[14] on the distribution of isotopic nitrogen (^{15}N) after feeding ^{15}N-glycine to rats. This work proved beyond doubt that there is, even in the adult animal, a constant and rapid turnover of many body proteins. Shemin and Rittenberg[15] later showed that the average life of rat liver protein was about seven days. Such rapid turnover is not, however, characteristic of all body proteins, since Neuberger and Slack[16] have recently shown that the rate of turnover of collagen in the adult rat is very low.

Enzymic Synthesis of Protein *in vitro*

When proteolytic enzymes are allowed to act upon protein in dilute aqueous solution, there is rapid hydrolysis of peptide bonds and liberation of small peptides and amino-acids. However, so long ago as 1901, Sawjalow[17] showed that when a concentrated solution of peptone was treated with fresh gastric enzyme there was formation of a precipitate which appeared to be protein in nature. This material was given the name 'plastein'. Even to-day, plastein formation continues to excite considerable interest as the simplest example of protein synthesis (cf. Tauber[18]).

The work of Bergmann and his colleagues, especially Fruton, on synthesis of small peptides by proteolytic enzymes has done much to clarify the mechanism of plastein formation. It is fundamental to the definition of an enzyme that it should be able to catalyse a reaction in both directions. For example, in dilute aqueous solution papain catalyses the hydrolysis of casein; but if papain is incubated with a concentrated solution of benzoylleucine and leucine anilide, a peptide bond is formed between the two leucines and benzoylleucylleucine anilide is precipitated from the solution:

$$C_6H_5.CONH.CH(R).COOH + NH_2.CH(R).CONH.C_6H_5 \rightleftharpoons C_6H_5.CONH.CH(R).CO.NH.CH(R).CONH\,C_6H_5$$

Benzoylleucine and leucine anilide are readily soluble in water, but benzoylleucylleucine anilide is very sparingly soluble. Papain catalyses the reaction in both directions, but the very low solubility of benzoylleucylleucine anilide in water causes immediate precipitation of the peptide as formed and the reaction is forced from left to right (Bergmann and Fraenkel-Conrat[19]).

During the past three years, Fruton[20] has shown that proteolytic enzymes also catalyse the exchange of one amino-acid for another within a peptide chain. Papain was incubated with carbobenzoxyglycine amide, leucylglycine and buffer. The enzyme catalysed the hydrolysis of the amide link in carbobenzoxyglycine amide, but not that of leucylglycine. When the reaction mixture was analysed it was found to contain 35 per cent carbobenzoxyglycine and 65 per cent carbobenzoxyglycylleucylglycine :

$$\text{Cbzo-NH.CH}_2\text{.CONH}_2 + \text{NH}_2\text{.CH}(R)\text{.CONH.CH}_2\text{.COOH} \rightleftharpoons \text{Cbzo-NH.CH}_2\text{.COOH} \quad (35 \text{ per cent})$$

$$\text{Cbzo-NH.CH}_2\text{CONHCH}(R)\text{.CONH.CH}_2\text{.COOH} \quad (65 \text{ per cent})$$

The enzyme had thus catalysed not only hydrolysis but also exchange of a peptide for a simple amide nitrogen. This transpeptidation, as it has been called by Fruton[21], shows that a proteolytic enzyme such as papain can act to lengthen a peptide chain provided that the necessary energy is available in the form of a preformed amide or peptide bond.

It is now reasonably clear that in plastein formation the concentrated solution of low-molecular weight peptides undergoes partial hydrolysis and partial transpeptidation, so that during the rather random rearrangement which takes place some peptide chains grow at the expense of others and eventually are precipitated as protein-like material.

Transpeptidation as a Mechanism for Protein Synthesis

It is known that all cells contain intracellular cathepsins, which are enzymes similar to papain, and it may reasonably be asked whether such enzymes could be responsible in part for protein synthesis. From our knowledge of the behaviour of proteases *in vitro* and from a knowledge of the thermodynamics of peptide-bond formation, it is possible to say at once that, if the intracellular cathepsins do take part in protein synthesis, they could only do so when provided with a supply of energy, probably in the form of a pool of preformed amide or peptide bonds. Study of amide-bond formation was initiated by the observation of Fuller[22] that sulphanilamide given by mouth is rapidly acetylated and excreted in the urine as acetylsulphanilamide. In 1945 Lipmann[23] found that a homogenate of pigeon liver could acetylate considerable quantities of sulphanilamide under aerobic conditions, but that anaerobically acetylation was slight unless adenosine triphosphate was added to the homogenate. In Lipmann's nomenclature, this suggested that energy for amide-bond formation was supplied by the energy-rich phosphate bonds of adenosine triphosphate. Borsook and Dubnoff[24] showed that adenosine triphosphate also stimulated formation of hippuric acid by guinea pig liver homogenates. Moreover, the formation of glutamine from glutamic acid by cell-free enzyme preparations was shown by Speck[25] and by Elliott[26] to require adenosine triphosphate. True peptide-bond formation as opposed to simple amide-bond formation has been studied by Bloch[27]. An extract was obtained from pigeon liver which catalysed the formation of glutathione from glutamylcysteine and glycine. For this condensation a supply of adenosine triphosphate was essential.

The exact mechanisms of these examples of amide- and peptide-bond formation are not understood, but it is clear that cells possess a variety of mechanisms for the conversion of phosphate-bond energy into amide or peptide bonds. Thus, from the thermodynamic point of view, there is no insuperable objection to supposing that protein synthesis takes place by transpeptidation catalysed by the intracellular cathepsins.

Attempts have been made during the past few years to obtain direct evidence for the conversion of simple amides and peptides into other peptides by transpeptidation. Waelsch[28] has shown that cell extracts can catalyse a reaction between glutamine and various amino-acids to give γ-glutamyl peptides. Hanes, Hird and Isherwood[29] have shown that kidney extracts catalyse formation of γ-glutamyl peptides from glutathione and various free amino-acids. In each case the product is a γ-peptide and not an α-peptide, and therefore the reactions are not quite satisfactory as examples of cellular transpeptidation from an amide-bond pool ; but further work along the same lines may well reveal other examples of transpeptidation or other amide-bond pools.

Objections to the Transpeptidation Theory

It should be clear from what has been said that there is much indirect evidence in favour of transpeptidation as a possible mechanism for protein synthesis. Evidence that a theory is possible should not be taken as proof that it is correct ; there are various observations difficult to reconcile with a transpeptidation mechanism.

It is obvious that, if protein synthesis takes place by transpeptidation, there should be present in cells a great variety of intermediate peptides, and we should expect that cells would find no difficulty in using for synthesis peptides supplied in their nutrient medium. Many experiments suggest that this is not so ; thus, for example, an animal can be maintained in positive nitrogen balance by intravenous infusion of suitable mixtures of amino-acids ; when a partial hydrolysate of protein is used instead of amino-acids, the animal appears to be unable to use much of the peptide material and this is rapidly excreted in the urine[30].

A similar difficulty arises in the study of the nutritional requirements of micro-organisms. Many organisms show loss of ability to synthesize one or other of the twenty amino-acids, but organisms have not been found with absolute growth requirements for peptides. Moreover, when a peptide has been found to have growth-promoting properties, this has usually been shown to be due to hydrolysis of the peptide (see ref. 55). Against this must be set a recent observation of Marshall and Woods[31] that the inhibition of bacterial growth by 4-methyltryptophan can be reversed by tryptophan peptides in a non-competitive manner. They suggest that 4-methyltryptophan inhibits growth by virtue of its ability to inhibit synthesis of tryptophan peptides ; thus a supply of peptide in the medium renders the organisms insensitive to 4-methyltryptophan. It must be

remembered also that, although there is little direct evidence of the use of peptides by bacteria, it is seldom that these organisms reach their maximal rate of growth except in complex peptide media[32].

It has frequently been claimed that, if peptides played any prominent part in protein synthesis, it should be possible to find peptides in cell extracts. No significant quantity of any peptide other than glutathione has ever been isolated from such extracts, but the value of this as evidence is extremely doubtful. It may be that proteolytic enzymes have no function in protein synthesis; but it is accepted that they must be responsible for intracellular degradation of protein. This degradation must take place by a stepwise process with production of numerous peptides, so that failure to isolate peptides is of no significance except as a demonstration of the inadequacy of our techniques.

Control of Specificity in Protein Synthesis: the Template Theory

Any scheme of protein synthesis must take into account immunological and chemical evidence that the proteins of each species appear to be unique and structurally distinct from those of other related species. To control synthesis in such a highly specific manner the transpeptidases would be required to show an extremely high degree of specificity. The work of the Bergmann school has shown that pepsin, trypsin, chymotrypsin and papain all have some specificity[33]. Each hydrolyses certain limited groups of peptides; but the recent results of Sanger[34] and of Desnuelle[35] suggest that proteases have different specificities when acting upon larger polypeptide chains. Their specificity in transpeptidation is still largely unknown.

If transpeptidation and coupling of many peptide units are the mechanism of protein synthesis, then many enzymes would be required for the synthesis of a single species-specific protein. These synthesizing enzymes would in their turn have to be synthesized by equally specific enzymes, so that we are faced with an infinitely receding series of enzymes controlling the synthesis of enzymes. However, the specificity of protein structure appears to be inherited within any one species, and the syntheses of proteins would appear, therefore, to be under genetic control.

So long ago as 1909, Bateson[36] suggested that there might be a connexion between genes and enzymes. The concept of the gene was originally a purely formal one, namely, that it is the ultimate unit of hereditary transmission; but in 1937 Haldane[37] suggested that genes had the dimensions of protein molecules. He pointed out that genes must be copied exactly in each succeeding generation and suggested that they behaved as master templates or moulds controlling the specificity of protein structure. This idea was extended still further by Beadle following his study with Tatum[38] of the effect of mutagenic agents on the bread mould, *Neurospora crassa*. After exposing a mould to X-rays, progeny could be isolated with changed nutritional requirements owing to inability to carry out one single step in the synthesis of an essential metabolite. The defect was inherited in a Mendelian pattern as though it were controlled by a single gene mutation, and was shown to be due to lack of a single enzyme. Beadle[39] suggested a one-to-one relationship between genes and enzymes. Since enzymes are proteins, it was a simple extension of this hypothesis to suggest that genes are master templates upon which proteins are synthesized, and that for each specific protein structure there is a template or gene.

Since the segregation of chromosomes during formation of the gamete cells exactly parallels the segregation of genes, it is reasonable to suppose that genes are located on the chromosomes. Both Brachet[40] and Caspersson[41] (using different methods) have shown that chromosomes contain much nucleoprotein and there appears to be good reason for supposing that the ultimate unit of self-reproduction, the gene, is composed either of nucleic acid or protein or an association of the two. Similarly, Stanley[42] has shown that the tobacco mosaic virus, another form of self-reproducing agent, is composed entirely of nucleic acid and protein. The same appears to be true of the bacterial viruses such as *Escherichia coli* phage[43]. Hershey and Chase[44] have labelled coli phage with radioactive phosphorus and sulphur and have shown that when the phage infects the bacterium only the radioactive phosphorus enters the cell and reappears in the phage progeny. Since phosphorus is associated with the nucleic acid fraction of the phage, it is reasonable to conclude that the nucleic acid fraction carries the inherited specificity of the virus. Emphasis on nucleic acid as the controlling factor in transmission of hereditary character and therefore of protein specificity has been increased by the demonstration that type transformation in bacteria can be brought about by cell extracts from other related bacteria and that the active factors in these extracts are nucleic acids[45]. The report of Binkley[45a] that cysteinylglycinase is a polynucleotide directly associates protein metabolism with enzymic activity in a polynucleotide.

In an attempt to take all these factors into account, Dounce[46] has recently outlined an ingenious theory of protein synthesis in which allowance is made for the close association between nucleic acids and inherited character. He suggests that nucleic acids function as templates in governing the order of arrangement of amino-acids in peptide chains as well as the order of nucleic acids in nucleic acid chains. It is supposed that the nucleic acid template is first phosphorylated to give a nucleic acid polyphosphate with a series of energy-rich phosphate bonds; this polyphosphate then reacts either with nucleoside or with amino-acids, thus giving either a double nucleic acid complex or a nucleic acid – amino-acid complex. Linear polymerization of the added nucleosides or amino-acids would then give either a complete replica of the original nucleic acid or a peptide chain, the specificity of which is dependent upon the nature of the original template of nucleic acid [see also p. 1027 of this issue].

This theory has several attractive features: it provides a mechanism for reproduction of the template or gene; it supplies an explanation of the genetic control of protein specificity by nucleic acid; it explains the failure to demonstrate any metabolic function for small peptides; and it provides a mechanism of energy supply for peptide bond formation. In spite of this, there are various facts which do not seem to fit any theory involving control of protein specificity by permanent nucleic acid templates acting as genes.

Objections to the Template Theory

Caspersson[41] has suggested that protein synthesis takes place at the nuclear membrane; but there is now no doubt that much protein synthesis takes

place in the cytoplasmic granules. London, Shemin and Rittenberg[47] have obtained synthesis of hæmoglobin in non-nucleated erythrocytes, and Brachet and Chantrenne[48] have shown that non-nucleated fragments of the marine alga *Acetabularia* can continue to synthesize protein for several weeks. Since proteins synthesized in the cytoplasm are undoubtedly species specific, the direct control of specificity of each protein by a nuclear gene acting as a template seems improbable.

The process of differentiation in higher organisms is also difficult to understand in terms of a controlling template in the nucleus. It would necessarily involve nuclear differentiation of the template, but this seems contrary to the assumption of a one-to-one relationship between templates and genes. There is, in fact, some recent work which suggests that nuclear differentiation does take place (Stern *et al.*[49]). Other apparent exceptions to the control of protein specificity by nuclear templates are adaptive enzyme formation in bacteria and antibody formation in animals. The adaptive enzyme is a new protein not only characteristic of the species but also characteristic of the substrate or inductor (Monod and Cohn[50]); while a new antibody is characteristic not only of the animal immunized but also of the antibody used for immunization.

It is frequently taken as proved that there is a direct correlation between nucleic acid synthesis and protein synthesis, but there is clear evidence that each can proceed in the absence of the other: according to Hokin[51], pancreatic slices can synthesize amylase without simultaneous synthesis of nucleic acid and indeed without turnover of nucleic acid phosphorus; according to Gale and Folkes[52] protein synthesis can be inhibited by antibiotics without simultaneous inhibition of nucleic acid synthesis.

The conception of the gene is essentially an abstract idea and it may be a mistake to try to clothe this idea in a coat of nucleic acid or protein. Perhaps the most striking of all immunological observations is the fact that, despite differentiation, an animal cannot usually be immunized against its own proteins. This would seem to support the idea that if we must have a gene it should have a negative rather than a positive function so far as protein synthesis is concerned. Expressed in terms of protein synthesis, this would mean not that all the proteins of an individual have some common structural pattern, but rather that they are alike in that they all lack some possible peptide sequence which other species have found it possible to synthesize.

Experimental Approach to the Study of Protein Synthesis *in vivo*

The advent of isotopic tracers and of improved chromatographic methods for the separation of amino-acids and peptides has made possible a more direct approach to the problem. As a suitable system for the study of protein biosynthesis, we have chosen the lactating mammary gland. Numerous earlier attempts have been made to determine the nature of the precursors of milk protein. By measuring the difference in amino-acid content between arterial blood entering, and venous blood leaving, the gland, it was concluded that little more than one-third of the milk nitrogen was supplied as free amino-acids[53]. If this is so, the mammary gland must be capable of transforming blood protein into milk protein, and it therefore seems to us that the gland was a particularly suitable organ for the study of protein biosynthesis (Campbell and Work[54]).

In preliminary experiments lactating rabbits were injected with radioactive amino-acids and the distribution of radioactivity in the blood and milk proteins was followed for seven days. If milk protein is derived from blood protein by minor transpeptidations, the injected radioactive amino-acids would not reach equilibration with intermediary peptides. In this case the radioactivity curves for blood and milk proteins would be expected to be of similar shape. In fact, it was found that the two curves showed no similarity, and that after six hours the milk casein was ten times more radioactive than blood plasma protein. From this result it was clear that the milk was synthesized largely if not entirely from free amino-acids. Other experiments using labelled radioactive plasma suggest that little of the free amino-acid is supplied by breakdown of plasma protein. It was noticed, however, that the casein was always more radioactive than the whey protein, and it thus seemed possible that casein was synthesized entirely from free amino-acids but that whey protein synthesis was by transpeptidation[55]. Whey is, however, a complex mixture of different proteins, and it was equally possible that some whey proteins were synthesized entirely from amino-acids and others obtained directly from blood protein.

By injection of radioactive methionine into an immunized rabbit, Campbell, Humphrey and Work[56] have recently shown that there is indeed direct transfer of antibody globulin from blood to milk; it thus seemed likely that this transfer would explain the low radioactivity of whey as compared to casein. To check this point, a lactating goat was injected with a mixture of four radioactive amino-acids and the milk collected four hours later[57]. The whey proteins were fractionated by the usual methods, and a β-lactoglobulin fraction was obtained which was electrophoretically homogeneous at *p*H 8·4. The radioactive amino-acids were re-isolated from this protein and compared with the corresponding amino-acids isolated from the casein. Valine and lysine were of the same activity in both proteins, but glycine, serine and methionine were less active in β-lactoglobulin than in casein.

It can be demonstrated on theoretical grounds that if two milk proteins are being synthesized on templates and from the same radioactive amino-acid pool, then the radioactivities of the amino-acids in the two proteins should be equal. The difference found between goat casein and goat lactoglobulin therefore suggested that peptides did, in fact, occur as intermediates in protein synthesis.

Distribution of Radioactivity at Different Points along a Peptide Chain

Let us suppose that protein is synthesized by stepwise coupling of many peptide units, some peptides being supplied by partial hydrolysis and transpeptidation of existing protein. After injection of radioactive valine, the protein formed would contain this amino-acid at various points along the polypeptide chain. At some points the valine would be derived from the pool of radioactive free valine, but at other points it would be derived from peptides containing valine which is not in equilibrium with

the free valine. There could thus be considerable variation in the activity of valine occurring at different points along the chain. If, on the other hand, the protein were synthesized by a template mechanism using only free amino-acids, there would be no substantial difference in the radioactivity at different points along the chain.

Muir, Neuberger and Perrone[58] measured the radioactivity of the terminal valine of rat hæmoglobin after injection of radioactive valine and found no difference between the terminal valine and the mean value for the valine from the remainder of the molecule. This result would be consistent with a template mechanism for globin synthesis. Askonas, Campbell and Work have carried out partial acid hydrolysis of radioactive casein obtained in the goat experiment already described. Preliminary results indicate a variation in the radioactivity of the valine in two different purified valine peptides and thus in activity at different points along the protein chain. In view of the fact that the valine isolations have to be made on a microgram scale, these results should be accepted only with considerable reserve, particularly since two serine peptides isolated from the same hydrolysate contained serine not differing significantly in radioactivity from the mean value for all the serine residues.

While this investigation was in progress, Anfinsen and Steinberg[59] were working quite independently along closely similar lines. They used as their protein-synthesizing system an oviduct mince, which appears to be capable of synthesizing ovalbumin. Radioactive carbon dioxide and radioactive amino-acids were incubated with this mince, and the distribution of radioactivity in the resultant radioactive ovalbumin was determined. Evidence was found for considerable differences in specific activity of alanine at different points along the chain. Again the results should be accepted with reserve, owing to the microgram scale of the work. It should be observed also that these results were obtained with a tissue mince in which transpeptidation could easily have occurred as an artefact; thus, they do not necessarily prove that ovalbumin is synthesized by way of peptide intermediates *in vivo*.

It is apparent from what has been said that there are two main streams of thought on protein synthesis: one derived from the study of isolated enzyme systems and suggesting a stepwise coupling of many small peptide units; the other based on the study of genetic inheritance of protein specificity and preferring synthesis on templates, each template being specific for a single protein structure and probably identifiable with a gene. It is impossible with our present knowledge to choose between these two theories. It may be that choice is the wrong word and that eventually a synthesis of the two ideas will be found to fit the facts. In the meantime, it seems certain that, by the application of such methods as ion-exchange chromatography and isotopic tracer techniques, much more can be learnt about the biosynthesis of proteins. Gale[60] has shown that in resting cells of *Staph. aureus* penicillin inhibits turnover of glutamyl residues of cell protein, but that in growing cells protein synthesis is insensitive to penicillin. It would be unwise, therefore, to assume that net protein synthesis is identical with protein turnover. If this is admitted, much of the apparent conflict between different types of evidence may well disappear.

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NEWS and VIEWS

Coronation Honours

The Coronation Honours list contains the following names of scientific men and others associated with scientific activities:

Viscount: Lord Woolton, recently Lord President of the Council.

K.C.B.: Sir John Cockcroft, chairman of the Defence Research Policy Committee and scientific adviser to the Minister of Defence, and director of the Atomic Energy Research Establishment.

K.C.M.G.: Sir James Hance, medical adviser and president of the Medical Board, Commonwealth Relations Office; Stephen E. V. Luke, comptroller for development and welfare in the West Indies and British co-chairman of the Caribbean Commission.

K.B.E.: Dr. John A. Carroll, deputy for research and development to the controller of the Navy and scientific adviser to the Board of Admiralty; Major-General Clive S. Steele, for services to engineering in Australia; Prof. Hugh S. Taylor, professor of chemistry and dean of the Graduate School at Princeton University.

Knights: Dr. Edward C. Bullard, director of the National Physical Laboratory; Sydney Camm, director and chief designer, Hawker Aircraft, Ltd.; Enoch B. Levy, formerly director of the Grassland Division, Department of Scientific and Industrial Research, New Zealand; George D. A. MacDougall, chief adviser, Statistical Branch, Office of the Paymaster General; Charles R. Morris, vice-chancellor of the University of Leeds; Thomas O. M. Sopwith, for services to aircraft production; Dr. Francis M. R. Walshe, president of the Royal Society of Medicine.

C.B.: R. Cockburn, scientific adviser to the Air Ministry; E. T. Jones, principal director scientific research (air), Ministry of Supply.

C.M.G.: J. Durward, deputy director, Meteorological Office, Air Ministry; Prof. G. Macdonald, professor of tropical hygiene, University of London, and director of the Ross Institute of Tropical Hygiene; G. W. Nye, deputy agricultural adviser to the Secretary of State for the Colonies; C. T. Saunders, deputy director of the Central Statistical Office, Cabinet Office.

C.B.E.: Prof. W. G. Barnard, professor of pathology in the University of London at St. Thomas's Hospital Medical School; F. S. Barton, principal director of electronic research and development, Ministry of Supply; A. G. Beattie, lately inspector-general of agriculture, Nigeria; A. D. J. Brennan, deputy chief veterinary officer, Ministry of Agriculture and Fisheries; R. L. Brooks, Colonial Forest Service, permanent secretary to the Ministry of Agriculture and Natural Resources, Gold Coast; J. N. Brown, assistant comptroller, Patent Office; R. W. Cheshire, deputy chief scientific officer, Admiralty; D. D. W. Cole, assistant controller (production), Atomic Energy Establishment, Risley, Ministry of Supply; W. J. Duncan, Mechan professor of aeronautics and fluid mechanics, University of Glasgow; A. Fage, superintendent of the Aerodynamics Division, National Physical Laboratory; J. E. Hurst, president of the British Cast Iron Research Association; R. G. Lloyd, secretary to the Royal Commission on Awards to Inventors; Dr. A. A. Miles, director of the Lister Institute of Preventive Medicine, London; A. McL. Mooney, deputy director of electrical engineering, Admiralty; D. A. Oliver, metals economy adviser, Ministry of Supply; F. Rayns, director of the Norfolk Agricultural Station at Sprowston, Norwich; F. H. Rowe, director-general, Commonwealth of Australia Department of Social Services; R. L. Scarlett, chairman of the Scottish Horticultural Advisory Committee; Lieut.-Commdr. P. M. Scott, director of the Severn Wildfowl Trust; P. M. Sherlock, vice-principal and director of extra-mural studies, University College of the West Indies; H. S. Young, deputy chief scientific officer, Ministry of Defence.

I.S.O.: F. R. Callaghan, secretary, Department of Scientific and Industrial Research, New Zealand; F. R. Ennos, senior principal scientific officer, Government Chemist's Department; W. R. Penhall, secretary of the Aborigines Protection Board, South Australia; E. F. Peck, Colonial Veterinary Service, director of agriculture and veterinary services, Somaliland.

Prince Louis de Broglie, For.Mem.R.S.

Prince Louis de Broglie was one of the four recently elected foreign members of the Royal Society. We owe to him one of the fundamental ideas forming the basis of quantum theory, the universal connexion between particles and waves. This connexion was obtained by de Broglie in 1924, apparently by a process of pure reasoning from mathematical relations suggested by relativity, and was for a while unsupported by any evidence, except in the case of light-quanta. However, it stimulated Schrödinger to seek for an explanation of the stationary states of atoms as a resonance phenomenon and led him to his famous wave equation, which is the accurate extension to curved orbits of de Broglie's relations for a particle on a straight course. In 1927 came the direct verification of de Broglie's ideas by Davisson and Germer working with slow electrons, and by G. P. (now Sir George) Thomson working with fast electrons, and a new era began in our understanding of atomic processes. The precise relationship of the waves to the particles remains a subject of controversy; what is established is that one must carry out calculations to determine the motion of the waves and then interpret them in terms of probabilities for the particles.

Geography at Leeds: Prof. A. V. Williamson

Another of the pioneers of university geography is retiring. It is much to be regretted that, for health reasons, Prof. A. V. Williamson is leaving the chair of geography in the University of Leeds, of which he was the first occupant. Trained in the school of geography in the University of Liverpool, he went to Leeds in 1922 as assistant lecturer when the department was small and struggling for adequate recognition. In 1927 he was given the title and status of lecturer as the department grew under his thoughtful guidance; and he became head of the department in 1928. His merits brought him the title of reader in 1933 and he was elected to the first chair of geography in 1944. By this time he had built up a large department which was continually outgrowing the accommodation available. Experience in the First World War widened his interests and directed particular attention to the East; but Prof. Williamson had no narrow outlook in his view of geography and no doctrines on the subject. Prof. Williamson also took a leading part in administration, taking his turn as dean of the Faculty of Arts and as a member

of the Senate and Council. To the deliberations of these bodies he brought penetrating criticism, sometimes caustic, but always valuable. He will be much missed by students and staff alike.

Linnean Society of London: Anniversary Meeting

At the anniversary meeting of the Linnean Society of London held on May 28, the Linnean Gold Medal was awarded to Prof. P. A. Buxton. The following were elected officers for the session 1953–54: *President:* Lieut.-Colonel R. B. Seymour Sewell; *Treasurer:* Colonel F. C. Stern; *Secretaries:* (Zoology) Dr. A. Tindell Hopwood, (Botany) Dr. George Taylor; *New Members of Council:* Mr. J. S. L. Gilmour, Prof. C. T. Ingold, Dr. L. Harrison Matthews, Dr. C. R. Metcalfe and Prof. E. Smith. Prof. Albert Dalcq, of Brussels, Prof. Alfred Sherwood Romer, of Boston, Mass., and Prof. Roger-Jean Heim, of Paris, were elected foreign members; and Robert Mackechnie and Douglas Miller Reid were elected associates *honoris causa*.

Bibliography of Scientific Aspects of Atomic Energy

The two volumes of "An International Bibliography on Atomic Energy", published by the United Nations Atomic Energy Section of the Department of Security Council Affairs, deal respectively with political, economic and social aspects, and with scientific aspects. Vol. 1 was issued in 1949 and Supplement No. 1 to this volume in 1950 (see *Nature*, 167, 671; 1951). In 1948 and 1949, preliminary mimeographed editions of the component parts of Vol. 2 were issued and circulated among experts of various countries, and in 1951 the printed edition was published. This volume, which listed more than twenty-four thousand articles, books and pamphlets published in all parts of the world during 1925–49, is divided into five main sections: fundamental nuclear science; the physics and engineering of nuclear reactors; the biological and medical effects of high-energy radiations; isotopes in biology and medicine; and applications of radioactive tracers in non-biological sciences and technology. However, the flow of scientific papers on nuclear energy has continued unabated, and periodical supplements to Vol. 2 have accordingly been planned, the first of which has recently been published (pp. 326. New York: U.N. Atomic Energy Section, Department of Security Council Affairs; London: H.M.S.O., 1952. 3.25 dollars, 25*s.* or 14 Swiss francs). The five sections into which it is divided are the same as in the original volume; but the table of contents has been somewhat improved in accordance with suggestions received, and fresh sub-divisions have been introduced to take account of rapidly growing or new research topics. The contents consist of 8,231 items, each item containing the authors' names, the title of the article (with translation if the original is in Russian), abbreviated title of the journal, the volume and page numbers and the date, and two appendixes (one an author index and the other a list of the journals, with addresses, arranged alphabetically under the abbreviations used in the volume). The bibliography does not exclude reviews and general articles, and in this respect is superior to some abstracting journals; but the absence of translations of titles in foreign languages other than Russian will cause difficulty to many users and will hinder further reference to abstracts in abstracting journals.

Institution of Professional Civil Servants

In his presidential address to the Institution of Professional Civil Servants at the annual delegate conference on May 18, Sir Richard Redmayne commented at some length on the position of the Department of Scientific and Industrial Research as indicated by that Department's recent annual report. The current estimates of the Department, he said, represent not a slight increase on the estimates for 1950–51, but a reduction of about ten per cent, and he urged that reductions in expenditure involving restriction of important and necessary work are not economy but waste. Sir Richard also referred to the Institution's intervention in the decision of the Ministry of Works to dismiss certain artist-craftsmen employed on the restoration of national art treasures, and the reversal of the decision after debate in the House of Lords. The annual report of the Institution's executive committee indicates its intention of seeking to improve the efficiency of the Civil Service by ensuring not only the proper employment of professional, scientific and technical officers, but also their full access to administrative posts on the bases envisaged in the Gardiner Committees' reports. It is also proposed to press (1) the claims for parity between the experimental and the scientific officer classes on one hand and the executive and administrative classes on the other; (ii) the technical grades salary claim deriving from the Gardiner report on the Works Group; and (iii) the salary scales for medical officers based on the Spens reports and the judgment of Mr. Justice Danckwerts.

Pacific Science Council Secretariat: Report for 1951–52

A report on the work of the Pacific Science Council Secretariat, covering the period March 1951–December 1952 (Bulletin *PS*/52/9; pp. 28; from the B. P. Bishop Museum, Honolulu, 1952), lists the continuing and completed projects of the secretariat, the supplements to the *Information Bulletin* issued during 1951 and 1952, and of the standing committees of the Pacific Science Association. The executive secretary represented the secretariat at the Australian National University's jubilee seminar on "Social Processes in the Pacific", and afterwards visited Singapore, Java, New Caledonia and Fiji. Reference is made to the value of the secretariat's assistance programme for transient scientific workers. The monthly summary, due for release in mid-January 1953, completed one full year of operation of the Pacific Area Communicable Disease Information Service; plague, small-pox, epidemic typhus, cholera, yellow fever, relapsing fever, all of which have already been reported by cable on a world-wide basis by the United Nations World Health Organization, are omitted to avoid duplication. The summary covers the reported incidence of more than thirty other diseases selected on the advice of health officers in the Pacific. A Periodicals Exchange Centre, covering periodicals published between 1920 and 1945, has been established by the secretariat jointly with the Unesco Science Co-operation Offices for South East Asia and for East Asia. The publication of a survey of Pacific scientific expeditions and of a handbook on organizations engaged in scientific research on an international scale in the Pacific was under investigation, while the secretariat was also responsible for organizing the Hawaii symposium on scientific research in the Pacific (held during March 9–10,

1951) and for preparing and distributing the papers and publishing the resolutions of the symposium. The admission of the Pacific Science Association to consultative arrangements with Unesco was approved by the sixth session of the general conference of Unesco (June–July 1951).

Museums and Education

In the January issue of the *Museums Journal*, Dr. D. A. Allan (of the Royal Scottish Museum, Edinburgh), who was director of the seminar on "Museums and Education" held at Brooklyn Museum, New York, during September 14–October 14, 1952, describes the work and activities of that important gathering. In all, there were thirty-eight members from twenty-four member countries, and the seminar was held under the auspices of the United Nations Educational, Scientific and Cultural Organization. It was agreed at the outset that museums have to save traditions and preach standards in a world where both are threatened. With labels and sympathetic guide-lecturers, there would appear to be no subject involving three dimensions that a museum cannot teach. Books and museum displays were regarded as complementary, but museums can make the great immediate appeal. Many speakers stressed that the development of the emotions is an important element in an individual's education and that here the art museum can achieve much by encouraging sensitivity, response and inspiration. From this the discussions emphasized, first, the value of atmosphere in the individual museum and, secondly, the value of a museum as a point of infection for its community. Museum services must be qualitative rather than quantitative, and warnings were expressed on the inadvisability of expert museum chiefs having to devote valuable time to obtaining financial support and the common fallacy that attendance figures reflect services given. The resolutions passed by the seminar stated the unanimous conviction of the value of museums and appealed for the fullest support for them as educational, cultural and recreational centres.

Calendar Reform

At the first meeting of the British Section of the World Calendar Association (20 Buckingham Street, London, W.C.2), which was held in London on October 17, Sir Harold Spencer Jones, the Astronomer Royal, gave a lecture entitled "The Calendar, Past, Present and Future". He began by pointing out that the difficulties in devising a satisfactory calendar have been due to the incommensurability of the three natural periods of time, the day, the month and the year, and he followed with a short survey of the various calendars—Egyptian, Babylonian, Greek, Jewish, Roman, Gregorian and Mahommedan—giving a brief reference to the confusion introduced by these different systems. In general, Sir Harold favours the adoption of the world calendar, which has the merit of being simple, stable and perpetual (see *Nature*, **169**, 961 and 1083; 1952). In this scheme, the year is divided into four equal quarters of ninety-one days, which would leave a day over in normal years and two days in leap years. Each quarter is divided into thirty-one, thirty and thirty days respectively, commencing with a Sunday and ending with a Saturday, and containing exactly thirteen weeks, the second and third months beginning on Wednesday and Friday, respectively. As there would be a day left over in normal years, this would follow December 30 and be named 'world day'; in leap years the other extra day would come in between the first and second halves of the year and be named 'leap day', and each of these days would be a world holiday. Religious objections which have been advanced against the scheme are not considered insuperable, and Sir Harold expressed the hope that the scheme, which is to be discussed by the United Nations Organization, will be seriously considered on its merits. He ended with an appeal for the widest measure of support for the world calendar, a reform which will only be possible if there is a vigorous campaign to expound its advantages to the ordinary man.

Careers in the Petroleum Industry

A number of booklets dealing with careers and prospects for professional men in the Royal Dutch/Shell Group of Oil Companies have been published by the Shell Petroleum Co., Ltd. (St. Helen's Court, London, E.C.3), and they can be recommended particularly to parents, headmasters and potential candidates for appointments in this field. In one, "Careers in the Petroleum Chemical Industry" (pp. 22; 1952), the subject-matter is divided into two sections, general information and careers. The former gives details of the Group's organization and work, incidence of National Service, conditions of pay, promotion, service overseas and how to apply for employment. Under the section on careers is explained the growth of this modern phase of petroleum technology, the marketing of special products, and areas where chemical manufactures are concentrated, concluding with a brief description of research and development laboratories, the production of intermediates and marketing areas. Another brochure, "Careers in the Royal Dutch/Shell Group" (pp. 82; second edition, 1952), goes into the oil industry in more detail, embracing the range of different occupations in the industry as a whole and covering all initial information that anyone having this vocation in mind will benefit by careful perusal. These publications are lavishly illustrated in a manner that, combined with excellent texts, brings home to the reader in straightforward wording the vast ramifications of this industrial scene as it exists to-day all over the world; no less are the great opportunities awaiting those who lean either to administrative or, perchance, more adventurous activities at home or overseas.

Guide to Chemicals used in Crop Protection

The number and variety of chemicals used in plant protection from insect pests, diseases and weeds has vastly increased during recent years. The nomenclature of the many compounds employed is most involved, and few would claim to be thoroughly conversant with them, while the rapidity with which progress in the subject continues renders it impossible for the text-book writer to keep abreast with the latest developments. Many will therefore welcome the issue by the Canadian Department of Agriculture of a publication entitled "Guide to the Chemicals used in Crop Protection", by H. Martin and J. R. W. Miles (pp. 236; from the Science Service Laboratory, University of Western Ontario, Sub Post Office, London, Ontario; 1952). This mimeographed publication gives a concise account of some 177 chemicals, including in each case their full structural formula, history, manufacture, properties (physical, chemical and biological), formulation and method of analysis. The arrangement is alphabetical and in loose-leaf form to facilitate addition or revision. An index is

also provided so that reference can be made by means of the alternative name if the full one is unknown. The precautions needed in the use of the compounds are stated where applicable.

Age and Evolution of the ζ Persei Group of *O*- and *B*-Type Stars

A PAPER on "The Age and Evolution of the ζ Persei Group of *O*- and *B*-Type Stars", by A. Blaauw, has been published in the *Bulletin of the Astronomical Institute of the Netherlands* (11, 433; 1952), and this follows up a previous publication (No. 363; 1944), in which the moving cluster of early-type stars including, among others, the bright stars ζ and ξ Persei, was described. Further studies, which are dealt with in the present paper, lead to some interesting conclusions with reference to the evolution of this group and to an estimate of the age of its members. The principal observational data concerning the stars of the group are contained in a table, and two figures show the adopted linear relation between the components of proper motion and the co-ordinates of the star. The slope of this relation is taken as a measure of the apparent expansion, and this relation should exist in the following circumstances: the present dimensions of the group are large compared with the dimensions at the time when the stars began their independent motions; and these motions started at the same time and have since been uniform. In the circumstances the linear relation is independent of the distribution of the sizes and of the directions of the velocities, and on the above two assumptions it was found that the time which has elapsed since the beginning of the uniform motions is 1·3 million years. It is admitted that this seems surprisingly short when compared with the period of revolution of the stars in the solar neighbourhood around the galactic centre—about 220 million years—or with the current estimates of the age of the sun. It would be possible to allow a longer time, however, if the condensation of the interstellar material into stars took place already during the process of contraction of the original cloud, but the difference would amount to only a few hundreds of thousands of years, so the figures given above must be accepted as approximately correct. In addition, the presence of high-luminosity stars like ζ and ξ Persei points to a small maximum age which can be estimated on the assumption of radiation of energy in the past proceeding at the same rate as at present, the source of the energy being the transformation of hydrogen into helium. Maximum ages of 7·9 and 7·4 million years for ζ and ξ Persei, respectively, are thus found, but for various reasons the true ages may be much less. An interesting feature of the group is the presence of a very small cluster of faint stars immediately south of o Persei, and the photographically determined proper motions for this cluster are shown in a table.

Latin American Course in Santiago on Electrophoresis

THE second of a series of international training courses, in collaboration with leading Latin American research institutions, in order to introduce and improve the use of modern techniques and methods in scientific research in Latin America, organized by the Unesco Science Co-operation Office for Latin America, was inaugurated in Santiago de Chile on April 20. The course, which was full-time and lasted for three weeks, dealt with electrophoresis and was attended by research workers from Argentine, Brazil, Chile, Colombia, Ecuador, Peru, Uruguay and Venezuela. The instructors for the course were drawn from the University of Chile with Prof. Dan H. Moore, head of the Laboratory of Electrophoresis of the College of Physicians and Surgeons, Columbia University, New York, as guest lecturer. The first of these courses dealt with the methodology of radio-isotopes in biological research and was held in the Laboratory of Radioisotopes of the University of São Paulo, Brazil, during January 14–February 28 (see *Nature*, February 14, p. 289). The next two courses planned by the Unesco Office will deal respectively with electron microscopy and chromatography, and further information can be obtained from Centro de Cooperación Científica para América Latina de la Unesco, Bulevar Artigas 1320, Montevideo, Uruguay.

Biology and Productivity of the Sea

A SYMPOSIUM on "The Biology and Productivity of the Sea" will be held, under the auspices of the Institute of Biology, in the rooms of the Royal Geographical Society during September 18–19. The subjects include zoology, botany, fisheries and oceanography, and papers will be contributed from the British Museum (Natural History); National Institute of Oceanography; Fisheries Laboratory, Lowestoft; Marine Laboratory, Aberdeen; Marine Laboratory, Plymouth; "Discovery" Investigations; Institute of Seaweed Research; Fisheries Experiment Station, Conway; Food and Agriculture Organization; Colonial Office. Other authors in Copenhagen, Malaya, Southampton and Cambridge are contributing. The chairmen of sessions are: Dr. E. Hindle, Prof. F. E. Fritsch, Dr. F. N. Woodward, Mr. F. S. Russell and Mr. H. J. Johns. Further information can be obtained from the General Secretary, Institute of Biology, Tavistock House South, Tavistock Square, London, W.C.1.

Announcements

THE Albert Medal of the Royal Society of Arts for 1953 has been awarded to Dr. E. D. Adrian, Master of Trinity College, Cambridge, for his outstanding contributions to neuro-physiology. This Medal, which is the highest award in the gift of the Royal Society of Arts, was instituted in 1864 to commemorate the presidency of the Prince Consort during 1843–61, and is given annually for "distinguished merit in promoting Arts, Manufactures and Commerce".

THE following appointments have been made in the Queen's University of Belfast: Dr. I. T. A. C. Adamson, formerly of Princeton University, to a lectureship in pure mathematics; Dr. A. R. Pinder, of Magdalen College, Oxford, to a lectureship in organic chemistry.

THE Heineman Foundation for Research, Educational, Charitable and Scientific Purposes, Inc., is offering a prize of 5,000 dollars, known as the "Dannie Heineman Prize", to be awarded every three years to the author of an outstanding book or manuscript in the mathematical or physical sciences. The object of the prize is to encourage the writing of books on a high scientific level which open up important fields of research. Those wishing to compete for the prize should submit two copies of the book or manuscript in question to the Secretary of the Foundation, 50 Broadway, New York 4, N.Y., not later than December 31, 1955.

ROCKETS

THE subject of rockets is one that has attracted considerable popular attention during the post-war years, but on which very little reliable technical information has been available. It was, therefore, an attractive and interesting topic for a discussion meeting on April 24 at the Society for Visiting Scientists. Introductory talks were given by the chairman, Prof. A. D. Baxter, Mr. I. Lubbock and Dr. A. C. Merrington, all of whom have had long experience in the rocket field, and afterwards a general discussion ranged over a wide variety of problems of scientific interest.

In opening the meeting, Prof. Baxter emphasized the propulsion side of the subject and reviewed the relationship of rocket propulsion to other forms of power plant. The major distinction is that the latter are air-swallowing; but the rocket motor is practically independent of the atmosphere. Consequently, the propelling force developed by piston engines, gas turbines and ram jets falls off as the altitude increases, whereas the rocket motor force actually increases slightly. At the same time, the dimensions of a rocket motor are very much less for the same thrust, and its compactness gives it advantages of low weight and air resistance. These are offset to some extent by the large consumption of propellant resulting from the need to carry its own oxidant. Such features make the rocket motor eminently suitable for short-duration propulsion at extreme speeds and altitudes; hence its role in aircraft, guided weapons and, in the future, space-craft. Because of the high fuel consumption, it is probable that new flight techniques will evolve as, for example, the use of a combined ballistic and extended glide path. These would introduce new problems—how to deal with the very high skin temperatures of the rocket at high speeds, the cabin air-conditioning for passengers, the physiological effects of prolonged accelerations and periods of weightlessness and so forth.

Mr. Lubbock, who followed, gave an account of the early methods of designing liquid propellant rocket motors, which were contrasted with those using solid propellants. The selection of an oxidant was made from the three best known: liquid oxygen, hydrogen peroxide and nitric acid. All three were used by the Germans during the Second World War and each has problems peculiar to itself. Liquid oxygen is attractive in many ways; but its low boiling point introduces engineering problems of storage and transfer to the combustion chamber. Conditions in the latter are much more severe than in other internal combustion engines—the gas pressure is at least 300 lb. per sq. in. and the temperature is of the order of 3,000° K., compared with the normal gas turbine maximum pressures and temperatures of approximately 80 lb. per sq. in. and 1,150° K. respectively. The thermodynamics of rocket combustion is therefore complicated by dissociation, and heat transfer calculations demand data well beyond the limits of experimental knowledge.

From this point, Dr. Merrington followed with an explanation of rocket motor testing and research procedure. Contrary to the usual ideas, he said, the greater part of the testing and development is done statically, and only in the later stages is it necessary to consider flight testing at one of the rocket ranges. As in most experimental work, some risk of component failure exists with new developments, and proper precautions have to be taken. The risks arise mainly from the concentrated potential energy of an unburnt propellant mixture. This energy is of the same order as in high explosives, and if its liberation is not controlled, explosion can occur. To reduce the consequences of this, static testing is carried out in reinforced concrete cells. Measurements of thrust, propellant flow-rate, and the associated liquid and gas pressures are made, but no satisfactory methods of measuring the high combustion temperatures have been devised. Because of the rapid rates of change in the quantities to be measured, especially during starting, electronic recording is frequently adopted. In flight, the operation of the motor is studied chiefly by telemetry, the main information required being obtained indirectly in the form of pressures recorded graphically.

In the discussion which followed, a variety of points were made and questions asked. There was a natural interest in any possible uses of rockets other than for warlike purposes. The best known has been the life-saving rocket, in operation for more than a hundred years, which carries a line from shore to ships in distress. Among others enumerated were the mail-carrying rocket which had been tried in places where the topographical features encouraged it, such as across mountain ranges or stretches of water, high-altitude sounding rockets for studying upper atmosphere conditions and, at the other end of the speed and height-scale, assisted take-off rockets for transport aircraft operating from short runways or in conditions where the main engines could not give sufficient thrust. Mention was also made of rocket techniques applied to the drilling of oil boreholes, the shaping of metal articles, and the operation of wind tunnels; the last relies on the ejector pump action of the high-velocity rocket exhaust gases entraining air from the tunnel. Such a tunnel would be expensive to operate frequently, but would save capital outlay on conventional electric motors and fans if only required intermittently. The principle has been applied to boundary-layer suction from aircraft wings to improve lift during take-off and landing. Another case of intermittent use requiring short periods of high-pressure gas generation is in driving small gas turbines used as engine starters.

The noise emitted by rocket motors was discussed at some length. This noise is made up from two sources—combustion and exhaust jet. Combustion noise is common to all types of engine in greater or lesser degree, and its level is dependent upon variables such as mixture ratio and combustion chamber loading. No satisfactory explanations relating the observed results in different forms of engine has yet been offered. Exhaust noise is a function of the shear velocity gradient between the jet and the atmosphere. Attempts to reduce this usually cause a loss of thrust. In cases where burning of fuel continued in the exhaust jet after leaving the motor, the suppression of this after-burning has produced a noticeable reduction in noise-level. Finally, it was remarked that, in most cases, rocket noise would be only of very short duration before the source would reach a height at which it would not be a serious trouble to ground observers.

The reliability of rockets, bearing in mind the *V2* firing failures, was queried; but it was stated that there is no fundamental reason why they should not be perfectly safe, and a number of aircraft applications were quoted in support. The problem of jettisoning assisted take-off or booster rockets in flight without damage to the motors or the populace below was also considered. A suggestion that rocket motors might be used for assisting gliders to extreme heights so that observations of meteorological interest could be made without the corrections necessitated by the transient conditions inherent in the sounding rocket was considered impracticable. An alternative proposal was a balloon with some rocket thrust available for directional control. Among other facts brought out was that the present maximum altitude reached by a rocket is 240 miles.

The chairman summarized the discussion by stating that rocket motors could give advantages wherever simplicity is needed, wherever high energy for short periods is demanded and wherever other power plants could not operate because of lack of air. The meeting then concluded with a short colour film of some rocket motor tests, both in flight and on the ground.

RADIOISOTOPE TECHNIQUES IN INDUSTRY

THE wide use of radioisotopes in medical research has received considerable publicity; but their field of application is by no means limited to medicine, and consultations between nuclear physicists conversant with radioisotopes, and workers in other branches of science and engineering soon reveal numerous important problems that can be tackled successfully by the use of these substances. The international conference on radioisotopes held during July 16–20, 1951, at Oxford, under the auspices of the Atomic Energy Research Establishment, Harwell, is an outstanding example of the value of such consultations. In all, ninety-eight papers were presented, grouped under the main headings of therapy and diagnosis, biochemistry, agriculture, and industrial and allied research applications, and divided into thirty separate sessions. The complete text of the proceedings of this isotopes techniques conference, including the chairmen's addresses, the papers presented and the discussions on them, is to be published in two volumes, the first of which, Vol. 2, covering Sessions 21–30 inclusive and devoted to industrial and allied research applications, has now appeared*.

For the first two Sessions, 21 and 22, dealing with general and metallurgical applications, Dr. B. Goldschmidt, of the Commissariat à l'Énergie Atomique, Paris, was in the chair, and in his opening remarks he expressed gratitude to Great Britain for the liberal policy adopted with regard to the release and distribution of radioisotopes for industrial purposes to foreign countries; in addition, he paid tribute to Dr. H. Seligman, the head of the Isotopes Division at Harwell, for initiating the conference. Of the seven papers presented in the two sessions, the two main ones were by Dr. Seligman on types of applications of radioisotopes, and by Dr. R. W. Cahn on radioisotopes applied to metallurgical research. Dr. Seligman briefly reviewed the various industrial applications, mentioning, in particular, gamma radiography, static eliminators and thickness gauges. He pointed out that tracers have not been used as extensively as they might have been, particularly in problems of process control. Dr. Cahn distinguished between what he called microscopic applications in metallurgy (such as tracer methods for the measurement of self-diffusion in metals, and autoradiography for the determination of tracer elements in alloy sections) and macroscopic applications, in which the normal experimental or industrial procedure is followed, but where, at some stage, tracer elements are introduced.

Session 23 was devoted to gamma radiography, and Mr. W. N. Blacklock, of the Ministry of Supply Aeronautical Inspection Directorate, who presided, referred to the prominent part taken by radiography in non-destructive testing. He stated that the present relatively inexpensive and abundant supply of radioisotopes largely eliminates the need for heavy and costly X-ray equipment for the testing of heavy metal components. Five papers dealt with gamma radiography tests of iron and steel castings and inspections of metal welds. These were preceded by an interesting short paper by Mr. W. S. Eastwood on the handling of radiographic sources, in which he mentioned that, in addition to radium and radon, only three radioisotopes—cobalt-60, tantalum-182 and iridium-192, all metals—are in current use. They are prepared by the Atomic Energy Research Establishment, Harwell, in the form of small cylinders of standard sizes. Shorter-lived isotopes are also obtainable; but these are irradiated to order at Harwell in the size required and to the necessary activity. With regard to transport of the strong sources, it has to be remembered that the limits of radiation at a package surface set by British Railways are even more stringent than those of airline companies, and thus radiographic sources are transported inland by motor-car and are sent to Continental users sometimes by sea.

Mr. B. Schuil, who spoke about radioisotopes in radiography and measurements of wall thickness, made an interesting reference to the psychological effect that radiographic control of welds has on welders who are working far away from their workshops. With radioisotopes, control and test of pipe welds are possible in the field even under the worst conditions, and it was found in Holland that when welders were aware that a radiographic inspection was in force the percentage of bad welds fell from 80 to 20 per cent. Finally, to wind up the Session, Dr. J. S. Blair described some of the safety precautions that are necessary when radioisotopes are handled.

In Session 24, on counting techniques, Dr. S. G. Cohen and Dr. D. Carmi described counters with thin plastic walls for the detection of X-rays, and Mr. H. Herne showed how, by the use of the commonly known, but not commonly employed, property of radioisotopes—namely, the random nature of the radioactive disintegrations themselves—the isotopes could be used in an analogue computer for stochastic problems. Mr. J. L. Putnam then discussed the very important but somewhat thorny problem of the absolute measurement of the activity of radioisotopes. He stressed the need for generally accepted standards of radioactivity and mentioned some of the intercomparison measurements and absolute measurements which are being made in

* Ministry of Supply. Radioisotope Techniques: Proceedings of the Isotope Techniques Conference, Oxford, July 1951, sponsored by the Atomic Energy Research Establishment. Vol. 2: Industrial and Allied Research Applications. Pp. iv+177+33 plates. (London: H.M.S.O., 1952.) 25*s.* net.

Britain. (Some of the results of these measurements have since been published; see *Nature*, **170**, 916; 1952.)

The study of solid reactions is probably one of the main applications for radioactive tracers in physical chemistry; and in Session 26, on chemical applications, the first paper, by Dr. R. Lindner, dealt with this subject. Another interesting paper in this Session, by members of the Kodak Research Laboratories, was on the determination of silver in photographic images using radioactive iodide (iodine-131). Where a large number of analyses is required, the radio-iodination method has a distinct advantage over the potentiometric method and is to be preferred where only a small image is available, as in X-ray crystallographic patterns, or when the optical density is low.

The remaining four Sessions (27–30) were devoted respectively to ion exchange, non-destructive testing, static elimination and radioactivation analysis. Mr. K. Fearnside, of Isotope Developments, Ltd., Aldermaston, described four instruments: the transmission beta-ray thickness gauge used in paper, plastic sheet and metal foil production; the reflexion beta-ray gauge for the measurement of the thickness of coatings and liquid films; the gamma-ray thickness gauge applied to thick or hot-rolled metal strip; and the package monitor used to check the contents of sealed packages as they leave the packaging machine. Mr. G. Syke dealt in more general terms with the problem of inspection and gauging with ionizing radiations. Fog-making on certain kinds of fabrics due to static electricity forming on the fibres can be prevented by dissipating the static when it occurs before it has time to become a nuisance. The static may be made to leak away either through the textile itself or through the surrounding air. Ionizing the air by means of a radioactive substance is a most successful method; and in his paper on radioactive static eliminators for the textile industry, Dr. P. S. H. Henry, of the Shirley Institute, discussed thoroughly the question of static on textiles and the relative merits of alpha- and beta-ray static eliminators. Finally, Mr. A. A. Smales gave some indications of the scope of radioactivation analysis, the essential basis of which is that an element is detected and determined by the formation of a radioactive nuclide which is then subjected to radioassay, and Prof. G. Chaudron described some work on the analysis of traces of sodium and copper in high-purity aluminium by pile activation.

BREEDING-BACK OF THE TARPAN

BEFORE the existence of human culture a number of different kinds of wild horses existed in Europe and Asia. Of these only one is extant to-day. This one was discovered by the Russian Przewalski in the desert-like steppes of Zungaria in western Siberia. Like most steppe-dwelling animals, the Przewalski wild horse is red-brown in colouring and light underneath. As a legacy from its forbears it still carries zebra-like stripes at the backs of the legs which show up very clearly in the summer coat. The discovery of the last remaining species of wild horse was followed by the news that in the 1920's it had become extinct in the free state. To-day only a few are left scattered in various zoological gardens, and none is breeding except in the sixteen-head Munich herd. It is on this herd that the hopes of preserving the species must rest.

If the species is not preserved, apart from its own interest, one of the most interesting animals of to-day will have become extinct. One of the European wild horses, the mouse-grey, for which the Russian name of tarpan has been adopted, was, in historical times, still extant over large areas of Europe (*Oryx* (Journal of the Fauna Preservation Society), **1**, No. 7; November 1952).

In the first half of the past century it was still numerous in the steppes of the Ukraine north of the Black Sea. In 1876 it became extinct, leaving few traces of its existence. The tarpan was different from the Przewalski wild horse not only in colouring but also in build. The Przewalski has strong thick bones and an almost disproportionately heavy skull with narrow forehead which, many investigators believe, is the reason why the heavy carthorses of to-day are descended from this type. The tarpan has much finer bones and a short light head and is probably the progenitor of swift riding horses.

Distinguished for his successful efforts in breeding back the wild aurochs, Heinz Heck, director of the Tierpark Hellabrunn, Munich, has also successfully bred-back the tarpan. Mares from Iceland and Gothland that were markedly like tarpans were crossed with a Przewalski stallion; the resultant crosses were mated with one another and, in 1933, from this stock emerged the first foal with a mouse-grey tarpan colouring. Other foals followed, and through resultant crossings there is to-day a considerable stock of back-bred tarpans in the Tierpark, Hellabrunn.

MICROSCOPY OF PLANT ASHES

THE statement that a microscope magnifies four hundred times never quite conveys a true idea of the wealth of detail that can be seen at this magnification. Perhaps only when the incredibly small fragments of material on a cosh, the minute amounts of blood or hair and other such negligible 'small dust of the balance', appear as important items of evidence in criminal proceedings is it realized how valuable is this instrument in the examination of such unpromising material.

One would, however, be pardoned in assuming that even the microscopist would have to admit defeat when dealing with material that had been so thoroughly incinerated that only an ash remained. However, in 1920, the Austrian botanist Hans Molisch investigated the structures left after incinerating plant material and showed that the ash still retained definite structural features. Prof. Gosta Edman, now professor of botany and pharmacognosy in the Royal Pharmaceutical Institute, Stockholm, was then a pupil of Molisch and later set out to investigate these 'ash pictures' systematically and has since published numerous papers on the subject. Recently he was awarded the Hanbury Memorial Medal of the Pharmaceutical Society of Great Britain which, in conjunction with the Linnean and Chemical Societies, periodically makes the award for "high excellence in the prosecution or promotion of original research in the Natural History and Chemistry of Drugs". After receiving the medal, Prof. Edman gave an account of his work on ash pictures (*Pharm. J.*, **170**, 189; 1953).

Naturally, a good proportion of the work has been concerned with powdered or broken vegetable drugs, and Prof. Edman claimed that his method of examination is sometimes more convenient than normal ones. The drug is strongly heated until the bulk of the tissues is completely burned away; the characteristic appearance of the mineral skeletons of the cell walls and the cell contents is then revealed. The method, however, has several other important applications, especially in criminal proceedings involving suspected arson. Further, the examination of prehistoric materials by this method has been of some assistance to archæologists. Thus, the examination of the charred vegetable matter in a Chinese clay-sheard, about five thousand years old, showed it to consist mainly of the remains of the leaf blades of *Oryza ativa*, the same plant used to-day for the production of rice. In the same way, fragments of cereals, medicinal herbs, etc., have been identified in the intestines of Egyptian mummies. Prof. Edman has also examined the ash pictures of about 375 related plant species in relation to their phylogeny and taxonomy and has published many original articles on this subject in the botanical literature. He concludes that extensive silicification of the cell wall is associated with primitive characters.

J. W. FAIRBAIRN

OBSERVATIONS AT THE ROYAL OBSERVATORY, GREENWICH

THE observations made at the Royal Observatory, Greenwich, during 1937 in astronomy, magnetism and meteorology, under the direction of Sir H. Spencer Jones, have been published in a single volume (pp. *A*62+*B*21+*C*200+*D*66+*E*46+40. London: H.M.S.O., 1951. £6 net), which is divided in five sections, *A*–*E*, as follows: meridian astronomy, equatorial observations, photo-heliographic observations, magnetic observations and meteorological observations.

The first section includes work on the transit circle and on the time service; in the former are the results of regular observations of the sun, moon, major planets and minor planets Juno, Ceres, Pallas and Vesta, and in the latter is given a short account of the new equipment and advances in the technique since the publication of the "Time Service Results" in 1936. The section on equatorial observations contains a table on the observations of double stars made at the Observatory which includes not only all pairs observed during 1937 but also all previously unpublished measures of earlier years. A systematic difference was found for close pairs between the results of the filar micrometer and of the comparison image micrometer (brought into use towards the end of 1937), and the table indicates which instrument was used.

The second section, on photo-heliographic observations, is by far the largest of the five sections. The positions and areas of sunspots and faculæ for each day during the year 1937 is the first of seven tables in this section, the photographs being taken at the Royal Observatories of Greenwich or of the Cape, and at the Kodaikanal Observatory (a negative transparency for November 3 was supplied by the Mt. Wilson Observatory to fill a gap in the series). The other tables are: a general catalogue of groups of sunspots for 1937; ledgers of areas and positions of groups of sunspots (recurrent groups and non-recurrent groups); total areas of sunspots and faculæ for each day; mean areas of sunspots and faculæ for each rotation and for the year; mean heliographic latitude of spots for each rotation and for the year; and observations of solar flocculi made with the spectrohelioscope.

The introduction to the section on magnetic observations describes the magnetic station at Abinger, with its instruments, methods of observation, magnetic reductions and arrangement of results; these results are listed in fifteen tables, and there are notes for each month of 1937 which briefly summarize the magnetic conditions exhibited by the traces of declination and horizontal and vertical intensity during the year. Finally, a description of the instruments and the meteorological reductions is given in the section on meteorological observations; several changes were made in the 1934 volume as regards the notation for clouds and weather, this being done to bring the symbols into general accordance with those in use at the British Meteorological Office.

All the above-mentioned work by the Royal Observatory, Greenwich, was continued during 1938, and an account of it has now been published; the volume is similar in all respects to that for 1937. Another series of Greenwich observations which has at last been published is Vol. 2 of "Observations of Colour Temperatures of Stars: Relative Gradients" (pp. 115; London: H.M.S.O., 1952; 25*s*. net); this volume covers the years 1933–38 and is a sequel to the observations of 1926–32, published in Vol. 1.

UNITED STATES NATIONAL ACADEMY OF SCIENCES

AT the annual general meeting of the National Academy of Sciences, held in Washington, D.C., during April 27–29, the following officers, new members and foreign associates were elected.

Vice-President: George W. Corner, director, Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland, for a four-year term.

New Members of Council: Edwin B. Wilson, professor of vital statistics, Harvard School of Public Health, Boston; and Hugh L. Dryden, National Advisory Committee for Aeronautics, Washington, D.C.

New Members: L. V. Ahlfors, professor of mathematics, Harvard University; P. Bailey, professor of neurology and neuro-surgery, University of Illinois School of Medicine; H. A. Barker, microbiologist, University of California, Berkeley; V. H. Benioff, professor of geophysics, California Institute of Technology; J. H. Bodine, professor of zoology, University of Iowa; L. Brillouin, director of electronics education, International Business Machines Corporation, New York; M. J. Buerger, professor of mineralogy and crystallography, Massachusetts Institute of Technology; H. E. Carter, professor of biochemistry, University of Illinois; D. M. Dennison, professor of physics, University of Michigan; J. P. Den Hartog, professor of mechanical engineering, Massachusetts Institute of Technology; J. W. M. DuMond, professor of physics, California Institute of Technology; C. Eckart, director of the Marine Physical Laboratory, University of California, San Diego;

R. Emerson, research professor in botany, University of Illinois; J. F. Enders, chief, Division of Infectious Diseases, Children's Hospital, Boston; P. J. Flory, professor of chemistry, Cornell University; G. Gamow, professor of theoretical physics, George Washington University, Washington, D.C.; V. Hamburger, professor of zoology, Washington University, St. Louis; C. E. Hille, professor of mathematics, Yale University; J. O. Hirschfelder, professor of chemistry, University of Wisconsin; J. G. Horsfall, director, Connecticut Agricultural Experiment Station, New Haven; E. H. Land, president, Polaroid Corporation, Cambridge, Mass.; D. P. C. Lloyd, member, Rockefeller Institute for Medical Research, New York; H. W. Nissen, associate director, Yerkes Laboratories of Primate Biology, Orange Park; D. Rittenberg, associate professor of biochemistry, Columbia University; J. F. Schairer, physical chemist, Geophysical Laboratory, Carnegie Institution, Washington, D.C.; T. Shedlovsky, member, Rockefeller Institute for Medical Research, New York; J. C. Street, professor of physics, Harvard University; M. Tishler, director, Development Research Department, Merck and Company, Inc., Rahway, N.J.; H. G. Wood, head of the Department of Biochemistry, Western Reserve University; and R. B. Woodward, professor of chemistry, Harvard University.

Foreign Associates: J. H. Oort, director, Leyden Observatory; and Wilder Penfield, professor of neurology and neurosurgery, McGill University, and director, Montreal Neurological Institute, Montreal.

KOSSUTH PRIZES IN HUNGARY FOR 1953

WINNERS of the 1953 Kossuth Prizes in Hungary, which are given for outstanding work during the past year, have recently been announced. These Prizes carry monetary awards of various amounts (1,000 forints is approximately £3), and those given for scientific, technological or medical work include the following. A Prize of 50,000 forints to Frederick Riesz, president of the Mathematical Section of the Hungarian Academy of Sciences, for his book entitled "Lesson of Functional Analysis", written in conjunction with B. Nagy, in which theories are developed that are of great importance in the development of mathematics. Prizes of 20,000 forints to B. Nagy, correspondent member of the Hungarian Academy of Sciences, for his part in the joint work with F. Riesz, mentioned above; F. Ratkovszky, for work on the electrification of the country and for making a 'diabolo-transformer'; K. Novobatzky, professor of theoretical physics in the University of Budapest, for research on the quantum theory; J. Egerváry, for work in applied mathematics on the theory of differential equations, particularly in the development of a method for computing the critical limit of rotations of rotors in turbo-generators; Z. Csürös, academician, for results achieved in the study of heterogeneous catalysis; A. Ábrahám, correspondent member of the Academy, for research of the nerve tissues, based on the teachings of Pavlov; Z. Gyulai, correspondent member of the Academy, for research work on the boundary layers of crystals and solutions, and for the production of artificial quartz crystals; V. Keilwert, chemical engineer at the Láng engineering factory for directing the planning of the Debrecne penicillin factory; J. Proszt, professor in the Inorganic Chemistry Institute, for pioneering research in the preparation of organic silicon compounds; L. Kulin, specialist in children's diseases, for results achieved in curing tuberculosis in babies; G. Bárczi, director of the Budapest Therapeutical Teachers Training College, for results achieved in basing Hungarian medical teaching and education on the natural sciences and for applying Pavlovian theories; J. Kollonitsch, departmental head of the Medicine Industry Research Institute, for medical research and work in the pharmaceutical industry, particularly in the new preparation of 'Treomycin' for the treatment of whooping cough, typhoid and dysentery.

Prizes of 10,000 forints to: P. K. Károly, correspondent member of the Academy, for his text-book entitled "The Factory Science of Electrical Machines", and for research; L. Verebély, professor at the Technical University, for his handbook entitled "Transmission of Electrical Energy", and for work on electrification; J. Urbanek, director of the Central Research Laboratory of the Electrical Industry, for his text-book entitled "Introduction to the Technical Science of Theoretical Electricity" and for his new method of cooling turbo-generators by refrigeration; S. Müller, correspondent member of the Academy, for work in organic chemistry in connexion with the industrial production of synthetic materials; A. Romwalter, university professor, for research in coal chemistry; K. Rauss, professor at the Pécs Medical Science University, for research into children's diseases and dysentery inoculation; L. Fuchs, university dean, for work on the theory of structural algebra.

HYDRATION OF METAL CATIONS

By Dr. E. GLUECKAUF and G. P. KITT
Atomic Energy Research Establishment, Harwell, Berks

MEASUREMENTS have been made by the isopiestic method of the water content of hydrogen and metal polystyrene sulphonates at different water vapour pressures and at two different temperatures, using concentrated sulphuric acid solutions as vapour pressure standards. This permits of a calculation both of water-activities (see curves *A* and *B*) and of the differential heats of hydration $\bar{H}$ of the ions (curve *C*). The polystyrene sulphonates of monovalent ions show in this respect great similarity to the behaviour of strong 1 : 1 electrolytes such as, for example, lithium chloride or perchloric acid and, as has been shown previously[1,2], can be considered as concentrated solutions of electrolyte in their swelling water. Indeed, the trend of $\bar{H}$ for the hydrogen polystyrene sulphonate (curve *C*) is very similar to that of concentrated sulphuric acid[2] in the range where the latter may be regarded as a monovalent acid, $H \cdot SO_4H$ (see curve *D*). For a study of concentrated solutions the polystyrene sulphonates have a great advantage over most aqueous solutions: they can be concentrated without crystallization to any desired strength (100 molal and above) and thus provide information on the interaction of water with all kinds

of ion at high concentrations which are normally attainable for acids only. The polystyrene sulphonate of very low cross-linkage (0·5 per cent divinyl benzene) was obtained by courtesy of Dr. K. W. Pepper, Chemical Research Laboratory (Department of Scientific and Industrial Research), Teddington.

Attempts to fit water-activity data of concentrated electrolyte solutions to a model have been made previously by R. H. Stokes and R. A. Robinson[4]. They found that the water 'adsorption isotherm' conforms to a Brunauer–Emmett–Teller type, and an indication was obtained that the hydrogen and lithium ions form a primary solvation shell of four firmly bound water molecules. Their evidence was based on experimental results for molecular water-to-ion ratios of $R > 3:1$ only, and thus could not give detailed information concerning the first three water molecules. Our experiments cover the cases of most monovalent cations for a range down to $R < 1:1$; in some cases hydration results go as low as $R < 0{\cdot}5:1$. So far, the experimental results have been evaluated for the H^+-resin only.

Over this much wider range, the results do not follow a Brunauer–Emmett–Teller isotherm and have to be interpreted as successive addition reactions of the type:

$$H\cdot(R) + H_2O \rightleftharpoons [H\cdot H_2O]^+ + H_1$$
$$[H\cdot H_2O]^+ + H_2O \rightleftharpoons [H\cdot 2H_2O]^+ + H_2,$$
$$\text{etc.,}$$

leading to mass law equations:

$$x_1 = K_1\cdot a_w\cdot x_0$$
$$x_2 = K_2\cdot a_w\cdot x_1,$$
$$\text{etc.,}$$

where x_0, x_1, x_2, etc., are the mol-fractions of ionic species containing 0, 1, 2, etc., molecules of water of hydration, and H_n are the heats of hydration.

The resulting isotherm has the form:

$$\frac{\text{mol } H_2O}{\text{mol ion}} = R = \frac{K_1a_w + 2K_1K_2a_w^2 + 3K_1K_2K_3a_w^3 + \ldots}{1 + K_1a_w + K_1K_2a_w^2 + K_1K_2K_3a_w^3 + \ldots}$$

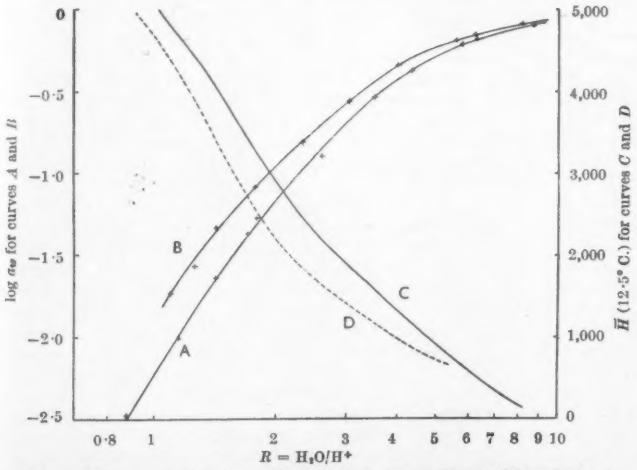
We obtain for successive water molecules the following values of K_n, ΔH_n, ΔF_n and the entropy:

$$\Delta S_n = \frac{\Delta H_n}{T} + R\ln K_n.$$

CONSTANTS (K_n), HEATS OF HYDRATION (ΔH_n), FREE ENERGIES (ΔF) AND ENTROPIES (ΔS) OF SUCCESSIVE HYDRATION STEPS

n	K_n (273°)	$-\Delta H_n$(285°) $= H_n$	$\frac{-\Delta F_n\,(273°)}{RT}$	$-\Delta S_n$
1	1,050	>6,000	6·96	>7·0
2	26·0	~4,500	3·26	9·3
3	5·0	2,000	1·61	3·8
4	3·5	1,400	1·25	3·4
5	1·48	1,000	0·39	2·7
6	1·24	700	0·22	2·0
7	1·12	400	0·11	1·2
8	1·06	250	0·06	0·9
9	1·03	150	0·03	0·5
10	1·015	100	0·015	0·3
etc.	→1	→0	→0	→0

The large number of constant K can be obtained from the single curve A quite accurately, as the first four constants each dominates a narrow region only. The knowledge of K and of the differential heats $\bar{H}$ (curve C) renders possible a calculation of the individual heats of reaction H_n and of the other thermodynamic constants. These results (see table) do not readily give the impression that, in concentrated solutions, four water molecules are firmly associated with the H^+ ion. There is a steady decrease both in the heats of reaction and in the free energies, and it requires some arbitrary assumption to differentiate between an 'association' and merely an attractive interaction. One could certainly not speak of an 'association' if the free energy of the reaction $-\Delta F$ is less than RT, and this places an upper limit on a hydration number of 4. But $-\Delta F = RT$ corresponds to a very loose association only, and if we stipulate that the free energy should exceed $2RT$ before we consider the association as a moderately firm one, we come to the conclusion that only two water molecules are firmly associated with the H^+ ion, and the second one much less firmly than the first.



Water activities a_w at 0° C. (curve A) and 25° C. (curve B) and differential heats of hydration $\bar{H}$ at 12·5° C. (curve C) as function of the ratio molar water to H-ion, R. For comparison, $\bar{H}$ for sulphuric acid solutions (curve D)

No doubt it is this uncertainty in deciding the degree of hydration which has led different authors to different conceptions about the hydration of ions according to the methods employed for estimating the 'hydration number'. (For a review on ionic solvation see ref. 5.) The present investigation shows clearly that the concept of a fixed hydration number is too crude, and has to be replaced by a quantitative description of the thermodynamic properties of the individual hydration steps.

It is interesting to speculate on the high values of the entropy changes during the first two steps, from which it appears that these steps are different from subsequent ones. The first water molecule obviously changes the covalently bound hydrogen to the ionized hydronium ion. Presumably the latter is strongly 'ion paired' to the sulphonate group of the resin, and the vigorous electrostatic interaction with the negative ion causes a reduction in the

number of possible configurations, which implies an increased entropy difference. Once the second hydration has taken place, the distance of the positive charge from the anion increases, and with it the configuration space and the freedom of rotation of the cation, as is shown by the steady decrease of the entropy differences with every further hydration step.

While some time must necessarily elapse before a detailed account can be given for a larger number of ions, it can already be stated from a cursory study of the experimental results that the same gradual decrease of the energies of hydration applies quite generally to all the alkali ions, to the alkaline earths, as well as to ammonium, silver and mercuric ions, and thus presumably is a characteristic feature of all metal cations.

This communication is published with the permission of the director, Atomic Energy Research Establishment, Harwell. [Nov. 20.

[1] Glueckauf, E., *Proc. Roy. Soc.*, A, **214**, 207 (1952).
[2] Duncan, J. F., *Proc. Roy. Soc.*, A, **214**, 344 (1952).
[3] Kunzler, J. E., and Glauque, W. F., *J. Amer. Chem. Soc.*, **74**, 3572 (1952).
[4] Stokes, R. H., and Robinson, R. A., *J. Amer. Chem. Soc.*, **70**, 1870 (1948).
[5] Bockris, J. O'M., *Quart. Rev. Chem. Soc.*, **3**, 173 (1949).

POTATO BLIGHT FORECASTING AND ITS MECHANIZATION

By Dr. JOHN GRAINGER
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THE fungus, *Phytophthora infestans*, causing potato blight, the most serious crop disease in Britain, has been shown by Beaumont[1] to begin its attack on the crop some 15–22 days after the occurrence of certain climatic conditions. These are a minimum temperature above 50° F. and a minimum relative humidity greater than 75 per cent, for a continuous period of at least forty-eight hours. During the past nine years I have used this method of forecasting with success in west Scotland when the recording instruments were near the potato crops (Fig. 1). It was, however, found necessary to establish a 'zero time'[2], before which suitable 'Beaumont' periods would not be regarded as valid. Zero time is July 1 for Ayrshire, but is a good deal earlier for the Atlantic islands. It would also be desirable to forecast the pattern and rate of blight development. Fig. 1 shows, however, that the ultimate build-up of this disease is not always closely linked with the occurrence of later 'Beaumont' periods. Experiments in Dumfriesshire and Perthshire suggest, however, that this difficulty may not be so important in practice as it appears in theory. When copper-containing sprays were applied according to blight forecasts in 1949 and 1950, increases in yield reached 28–30 per cent. These figures are high, for the average increase in overall crop cannot have been more than 20 per cent when sprays were given indiscriminately. Forecasts can introduce an important degree of precision into protective spraying, for blight cannot establish itself on foliage already coated with copper-containing sprays.

The time of first appearance of blight is also important in another special connexion, namely, the lifting of Epicure 'seed' in Ayrshire. This is usually

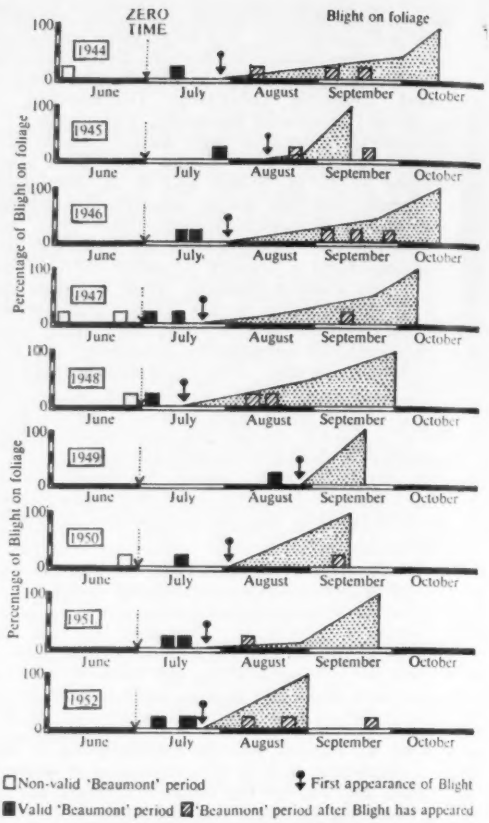


Fig. 1. The occurrence of suitable climatic ('Beaumont') periods and the average development of blight at Auchincruive during 1944–52. Where two valid periods are shown (1946, 1947, 1951 and 1952), the first would have been the operative one

done in July, during which month the disease appeared in five out of the nine years mentioned in Fig. 1. Even small amounts of blight on the foliage when the crop is lifted infect the tubers, and storage losses are heavy. This type of infection can be prevented by destroying the foliage with sulphuric acid, sodium chlorate or by mechanical means, and waiting a fortnight before lifting. Blight forecasts would advise the farmer as to whether this operation were necessary or not, and here again they would bring precision to control operations.

Forecasts of the first appearance of blight are therefore useful in practice and can be made satisfactorily when recording gear is near a potato crop. It is, however, necessary to extend such a service to cover all potato crops in a given region. A certain measure of success has been obtained over the past three years for wider areas of the west of Scotland, in issuing unofficial forecasts based upon conditions reported by telephone from meteorological stations attached to aerodromes. This has been a most effective co-operative effort, and its only demerit is that the aerodromes are not near the largest potato-growing areas. It becomes increasingly obvious that a greater number of reporting stations is needed in closer relation to the crops if blight forecasting is to become a fully practical proposition.

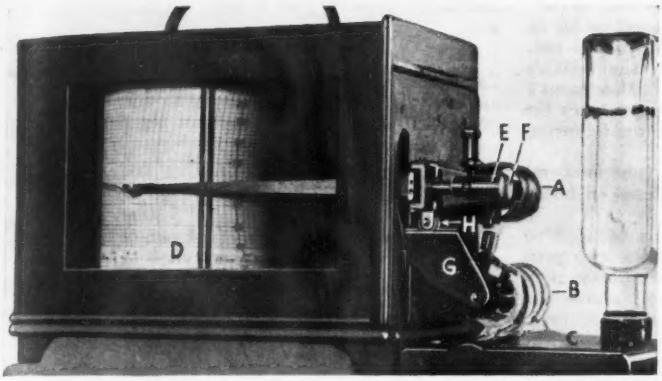


Fig. 2. The 'Auchincruive' self-calculating blight forecast recorder. For explanation of lettering, see text

Temperature can, of course, be recorded adequately by means of a bi-metallic thermograph, and even more accurately with a mercury-in-steel recorder. Relative humidity can be recorded directly by means of a hair hygrograph and by the Gregory humidity recorder; the first is temperamental, the second costly. Duplex wet- and dry-bulb instruments have the demerit that they record only temperature and the depression of the wet bulb, but not the actual percentage relative humidity. Successful forecasts of potato blight have nevertheless been made with such an instrument by Sir James Denby Roberts at Strathallan, Perthshire. Interpretation of the difference between the two traces for a relative humidity of 75 per cent or more is, however, rather difficult, because the depression varies with different temperatures. At 50° F., however, the depression of the wet-bulb reading for this humidity is 3·5° F. If, therefore, the two records are separated by less than this amount for forty-eight hours on end, it is fairly safe to forecast an outbreak of potato blight, provided the dry-bulb temperature is not much above 50° F. Another difficulty is that the two pens are set to record two hours distance apart on the chart, so that considerable skill is required in interpreting this differential comparison. There is thus a need for a forecast recording instrument which could be read and interpreted easily, accurately, and without special skill.

Figs. 2 and 3 show details of an inexpensive, accurate and easily interpreted instrument in which the recording elements are bi-metallic coils. Temperature is recorded in red ink by means of a pen (*E*) driven directly by a dry-bulb coil (*A*). A 'calculator'-pen (*F*), operated in a special manner from a wet-bulb coil (*B*), and marking in green ink, is so calibrated in relation to the temperature-pen that the lines they trace upon a rotating chart drum (*D*) will coincide at the relative humidity of 75 per cent, no matter what the temperature. Calibration of the instrument for this special purpose is done while the 'wet-bulb' coil is dry, when the calculator pen (*F*) is set to record higher than the temperature-pen (*E*). The higher reading is made equal to the depression of the wet-bulb temperature for 75 per cent relative humidity. This depression, and therefore also its corresponding higher reading, vary with different dry-bulb temperatures (see table). The varying higher reading is brought about by means of a cam (*G*) of special shape, driven by the 'wet-bulb' coil, and operating the calculator-pen through a roller movement (*H*) (Fig. 3).

The cam, though made of a single piece of metal, can perhaps best be thought of as having two parts—a basic section and a calculator section, which integrate two kinds of motion. The basic section, if used by itself, would impart a motion to the calculator-pen exactly similar to that of the directly driven temperature-pen for similar conditions around the coils which operate them. Added to the basic section, however, is the wedge-shaped calculator part (shown black in Fig. 3) which is responsible for the varying higher reading mentioned above. The working face of the cam is actually a very slight curve, to reflect the relation (not quite linear) shown in the table, and also the fact that the basic section edge would not be exactly a straight line.

Dry bulb temperature (°F.)	20	30	40	50	60	70	80	90
Depression of wet-bulb reading for 75 per cent relative humidity in louvre screen (°F.)	1·5	2·2	2·8	3·5	4·2	5·0	5·8	6·6

When the instrument is in operation, the wet-bulb coil is kept wet by a muslin sleeve fed by wicks dipping into the water reservoir (*C*). The calculator-pen then reads lower than its calibrated value, and, when the relative humidity is exactly 75 per cent, this depression due to evaporation-cooling of the wet-bulb coil equals the higher setting brought about by the calculator part of the cam. Calculator-pen records (green) are therefore on the same line as the temperature-pen records (red) for the particular relative humidity of 75 per cent, no matter what the dry-bulb temperature may be. Similarly, if the relative humidity is greater than 75 per cent, the

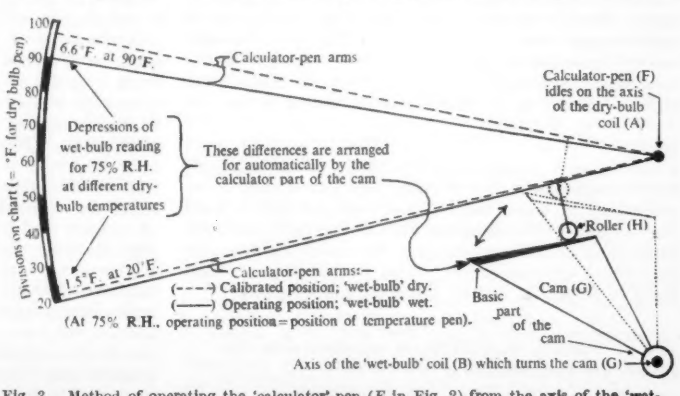

Divisions on chart (= °F. for dry bulb pen)
100
90
80
70
60
50
40
30
20
6.6°F. at 90°F.
Calculator-pen arms
Calculator-pen (F) idles on the axis of the dry-bulb coil (A)
Depressions of wet-bulb reading for 75% R.H. at different dry-bulb temperatures
These differences are arranged for automatically by the calculator part of the cam
Roller (H)
1.5°F. at 20°F.
Calculator-pen arms:—
(- - - -) Calibrated position; 'wet-bulb' dry.
(——) Operating position; 'wet-bulb' wet.
(At 75% R.H., operating position = position of temperature pen).
Basic part of the cam
Cam (G)
Axis of the 'wet-bulb' coil (B) which turns the cam (G)

Fig. 3. Method of operating the 'calculator'-pen (*F* in Fig. 2) from the axis of the 'wet-bulb' coil (*B*)

evaporation-cooling of the 'wet-bulb' coil is not sufficient to cause the calculator-pen to fall as far as the temperature record, and green reads above red. Conversely, if green reads below red, the relative humidity is less than 75 per cent. Beaumont's specification[1] of the climatic conditions necessary for a blight forecast are therefore given by the following simple rule:

Green (calculator) on or above red (temperature) and both on or above 50° F. for at least 48 hours on end.

The lag between the two records is reduced to minute proportions by arranging that the two pens only just clear each other. A blight forecaster may be placed within a louvre screen 4 ft. above the ground, or it may be placed in an aspirated screen if an electric fan is available to draw air over the elements. While the self-calculating mechanism as described is here worked from bi-metallic coils, it is equally applicable to mercury-in-steel recorders.

Protective spraying against blight is fully economic in many parts of Britain; but in some areas tuber production is usually complete by the time the disease destroys the foliage, and losses in overall yield are insufficient to balance the expenditure on sprays. Even in such districts, however, any factor which might delay planting in spring retards the growth-cycle, and protective spraying then becomes economic. Blight forecasts are thus of wide application in the improvement of control of this most widespread and severe crop disease.

[1] Beaumont, A., *Trans. Brit. Mycol. Soc.*, **31**, Nos. 1 and 2, 45 (1947).
[2] Grainger, J., *Trans. Brit. Mycol. Soc.*, **33**, Nos. 1 and 2, 82 (1950).

X-RAY INACTIVATION OF POLYPLOID *SACCHAROMYCES*

By W. H. LUCKE and A. SARACHEK

Biological Research Laboratory, Southern Illinois University, Carbondale, Illinois

THE recent development by C. C. and G. Lindegren[1] of a family of polyploid yeasts provides the first opportunity of establishing the influence of polyploidy on X-ray inactivation through survival curve analysis. These analyses show that in each cell a single target sensitive to X-rays exists for each chromosome set.

Since polyploidy involves the replication of genetic units, interpretation of the survival curves on a multi-target basis is suggested. The multi-target theory[2] postulates that there is a number of independent targets in the cell, the probability that each target survives a dose D of radiation being

$$P_t = \exp -KD,$$

where K is a constant independent of cell concentration and dose. It is further postulated that there are n sets of these targets (we shall identify n with the number of chromosome sets in the cell), each set containing m different targets (for example, genes or individual chromosomes). The probability θ'_i that the i'th target in one of the n sets is killed is

$$\theta'_i = (1 - \exp -K_iD).$$

The probability that all the n repetitions of the i'th target are inactivated is

$$\theta_i = (1 - \exp -K_iD)^n,$$

and the probability that at least one of them survives is

$$S_i = 1 - (1 - \exp -K_iD)^n.$$

Expanding the term in parenthesis by the binomial method, and confining ourselves to doses such that powers of $\exp -K_iD$ higher than the first may be neglected, we have:

$$S_i = 1 - (1 - n\exp -K_iD)$$

$$S_i = n \exp -K_iD.$$

Then the probability that at least one of the n alleles of all the m kinds of targets survives is:

$$S = \prod_{i=1}^{i=m} n \exp -K_iD.$$

Taking the logarithm:

$$\ln S = m \ln n - D \sum_{i=1}^{i=m} K_i. \qquad (1)$$

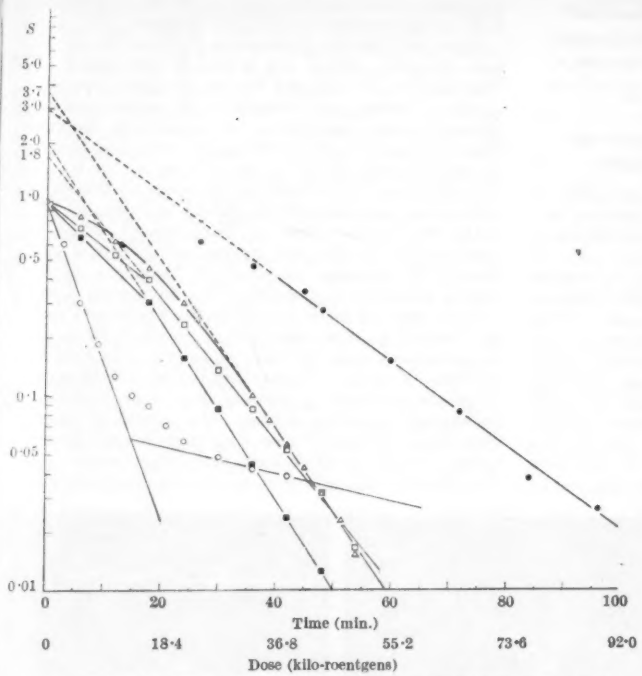
Extrapolation to zero dose gives

$$\ln S = m \ln n.$$

The experimental results are in agreement with equation (1) only for $m = 1$ and n equal to the number of chromosome sets per cell. Under these conditions, all slopes should be equal. While the diploids and the tetraploid have the same slopes, the haploid is about twice as sensitive and the triploid twice as resistant. These figures have been confirmed independently by Pomper and Atwood (personal communication).

A triploid organism was obtained by mating the haploid gamete 13,894 and the diploid gamete 11,296, and a tetraploid was obtained by mating the two diploid gametes 11,294*aa* and 11,296*αα*. Gamete and hybrid clones were grown for 24 hr. on peptone–glucose slants and then refrigerated at 4° C. to serve as stock inocula. Samples of yeast were prepared for irradiation by transferring a heavy loop of cells from a stock inoculum to a 250-ml. flask containing 25 ml. of clarified *V*-8 juice (*p*H 3·9), a commercial mixture of several vegetable juices. After 44–48 hr. growth on a rotary shaker at 30° C., the cells were harvested, washed twice with 1/15 *M* potassium dihydrogen phosphate and resuspended in 1/15 *M* potassium dihydrogen phosphate to a cell count of approximately 5×10^5 cells per ml. Under these conditions, the cells were in a nearly uniform physiological state as indicated by the absence of budding and detectable reserves of glycogen and volutin, and the presence of a complement of numerous prominent mitochondria.

A quantity of 30 ml. of the suspension was transferred to a sterile Petri dish and irradiated by X-rays from a tungsten target tube operated at 180 kVp. at a rate of 920 r./min. as measured with a Victoreen 2,500 r. chamber. The total filtration was 3 mm. of aluminium. The suspension was agitated by means of a magnetic stirrer during irradiation. Exposures were made for successive 6-min. intervals. After each exposure a 1-ml. sample was removed, diluted in phosphate and plated in duplicate (controls in quadruplicate) in the following medium: 0·2 per cent Budweiser yeast extract, 0·1 per cent ammonium sulphate, 2·0 per cent dextrose, 0·15 per cent potassium dihydrogen phosphate, 0·05 per cent magnesium sulphate, and 2·0 per cent agar. Percentage survival was determined for each exposure by average macroscopic colony counts after incubation for three days at 30° C.



○—○—, Haploid (13,894), slope = 0·19; ■—■—, diploid (11,296), slope = 0·11; □—□—, diploid (11,294), slope = 0·086; ●—●—, triploid (13,894 × 11,294), slope = 0·050; △—△—, tetraploid (11,294 × 11,296), slope = 0·10

The points for the survival curves shown in the accompanying graph are averages of the survival values for the corresponding dosage as obtained from a number of independent determinations: five for the haploid; six for the diploid 11,294; four for the diploid 11,296; six for the triploid; and six for the tetraploid. Values for the extrapolate and slope were obtained by fitting the straight line portion of the curves by the method of least squares to the equation

$$\ln S = A - KD,$$

where S is the surviving fraction, A is the natural logarithm of the extrapolate, K is the slope and D is the dose expressed in minutes of exposure.

The average survival curves for haploid, diploid, triploid and tetraploid give extrapolates of 1, 2, 3 and 4, respectively (see graph). The extrapolates of individual survival curves were in general well reproducible. The scatter was small, and a good estimate of the extrapolate could be obtained by eye.

The experimental results indicate clearly a one to one correspondence between the degree of polyploidy and the number of targets per cell. It is not possible to state whether the target is a physical part of the chromosome set or is a consequence of the presence of the chromosome set.

An attempt to identify the target leads to the following considerations.

(1) Significant killing by the induction of dominant lethals is eliminated by the occurrence of extrapolates greater than one.

(2) If m is taken to represent the number of genes per chromosome set, the experimentally determined value of unity eliminates recessive lethal mutation as an important aspect of inactivation in the polyploids, although recessive lethal mutation may account for the discrepancy between the haploid slope and the diploid and tetraploid slopes.

(3) If one assumes that all chromosomes have approximately the same sensitivity, and m is taken to represent the number of chromosomes per set, the possibility that inactivation is due to the destruction of homologous chromosomes is eliminated as an important factor, since it is known that there are at least four chromosomes per set in *Saccharomyces*[3].

It may be suggested that the target is a particular chromosome in each set. This hypothesis evidently demands that the chromosome in question be be enormously larger than all the others or much more sensitive. The loss of a very large chromosome, however, would lead to an unbalance which would probably be lethal. The occurrence of an unusually sensitive chromosome seems unlikely in view of the demonstration of the equivalent break sensitivity per unit length in *Drosophila* chromosomes[4].

(4) Inactivation may be due to the destruction of a non-genic target. It is generally observed[5] that inactivated cells undergo several divisions before growth ceases. This indicates that the primary damage is not upon an enzyme or enzyme system but rather upon nuclear entities mediating their production and maintenance. The nucleolus and the central body are two vital extra-chromosomal structures associated with the nucleus. The central body is an unlikely target, since, in general, one exists per nucleus regardless of the degree of polyploidy. In polyploid *Saccharomyces*, it is not known at present whether a single nucleolus exists for each chromosome set or whether the several nucleoli are fused into a single body. Assuming that one nucleolus does exist for each chromosome set, the probability of hitting all nucleoli should not be greater than the probability of hitting homologous chromosomes, since there is no evidence that the nucleoli are significantly larger than the chromosomes.

It is known that radiation causes simultaneous damage to individual genes, enzymes, chromosomes and other organelles. While there is a remote possibility that the total of these damage factors is insignificant in comparison with damage to an as yet unidentified cellular structure, it is more probable that the observed integral extrapolates are expressions under the influence of polyploidy of an unusual inter-relation of these factors.

This work has been supported by research grants from Southern Illinois University, the U.S. Atomic Energy Commission, and Anheuser-Busch, Inc.

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LETTERS TO THE EDITORS

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Statistical Nature of 'Facilitation' at a Single Nerve-Muscle Junction

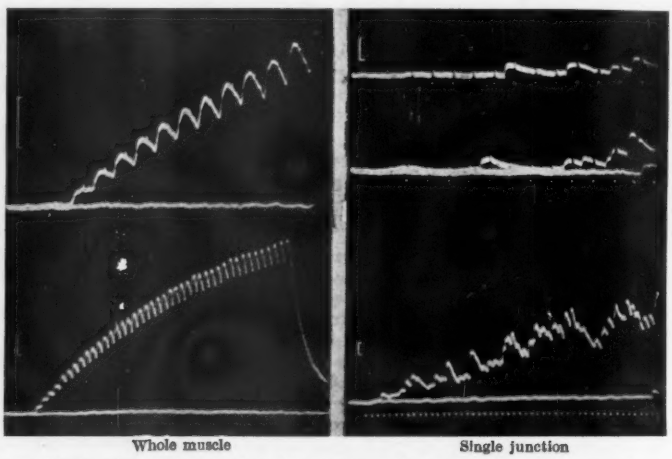
When an impulse arrives at a motor end-plate, it causes acetylcholine to be released at numerous 'key points' and in discrete quanta, each containing a large number of molecules[1]. The discharge of each quantal unit is an all-or-none event, and its success or failure is subject to independent statistical fluctuation. Its chances can be altered by various means, for example, by changing the ionic environment. Even under normal conditions, the probability of an individual 'quantum response' appears to be less than unity; that is, a nerve impulse excites at each junction only a fraction of the whole synaptic population. By lowering the calcium and raising the magnesium concentration, the chance of any one unit responding to a nerve impulse can be reduced to a very low value, and under these conditions, which apply to all the experiments described below, the statistical nature of the transmission process can be demonstrated most effectively.

It has previously been shown that individual quantal units discharge spontaneously, in the absence of nerve impulses[1]. This enables one to measure the mean unit size, and to determine the average number (m) of quanta responding to one impulse. Provided m is not too large, it is given simply by the ratio (mean amplitude of response)/(mean amplitude of spontaneous potentials). When m is a small number (the probability of each quantum response being very low), the actual numbers (x) in a large series of observations are found to vary at random and to be distributed in accordance with Poisson's law (their relative frequencies being given by $\exp(-m)\, m^x/x!$). The proportion of failures in such a series is $\exp(-m)$; hence the following relation is obtained:

$$\frac{\text{Mean amplitude of response}}{\text{Mean amplitude of spontaneous potentials}} = \ln \frac{\text{No. of nerve impulses}}{\text{No. of failures of end-plate responses}}$$

For example, Fatt and Katz (ref. 1, Fig. 9 and p. 120) described a case of a calcium-deficient end-plate at which 328 nerve impulses elicited 140 end-plate potentials, made up mostly (about a hundred) of single units, the remainder containing two or three quanta. The mean amplitude of 328 responses (including 188 failures) was 0·495 mV.; the mean size of spontaneously occurring potentials (that is, the mean unit size) was 0·875 mV.; hence $m = 0{\cdot}495/0{\cdot}875 = 0{\cdot}57$. From Poisson's law, for $x = 0$, $m = \ln 328/188 = 0{\cdot}56$. Thus, the statistical *average* response in this experiment consisted of less than one quantum per impulse, the observed responses showing a wide, discontinuous variation of amplitudes and a high proportion of total failures.

Some well-known phenomena such as 'facilitation' and 'fatigue', which are generally associated with transmission of impulses across synapses, appear to involve a progressive change in the mean number of quantal units responding to successive impulses. Thus we found with intracellular recording that the second of a pair of nerve impulses, at a time interval of 5–10 msec., produced an increase of 50–80 per cent in the mean size of the end-plate potential. This is the well-known effect of 'facilitation'[2], which has been studied in the past by recording from a whole muscle the average response of hundreds of end-plates, arranged in parallel. We have used a more tedious method of determining the statistical mean, by measuring the average size of hundreds of successive responses from a single end-plate. In this way we found that the increased amplitude of the second end-plate potential is entirely due to an increase of its average quantum content, the second of the two responses following a Poisson series with a significantly lower proportion of failures and larger value of m. The chances of excitation of any one unit remained small, but were 50–80 per cent greater for the second of the two nerve impulses. It can be shown that this increased probability does not depend upon there having been a previous response of any unit; and that, in general, the particular units activated by the second impulse are not the same as those responding to the first.



Facilitation of end-plate potentials at the nerve-muscle junction. The records were from nerve–muscle preparations of the frog, blocked by the use of high magnesium (14 mM/l.) and low calcium (0·9 mM/l.) concentrations, during repetitive stimulation of the nerve at 100 impulses per sec. (in the right part, stimuli are marked by dots). Bottom records were taken on slower time base. Left: Surface recording from a junctional zone of frog's sartorius. Right: Intracellular records from a junction of a muscle fibre of M. ext. l. dig. IV. Note the single spontaneous discharges occurring at the end of the 'base-line' sweeps. Scales: 1 mV.

The statistical nature of 'facilitation' is further shown in the accompanying records. On the left side are records of end-plate potentials obtained with the usual method of surface recording from a whole sartorius muscle. They illustrate that during a rapid firing of nerve impulses, at 10-msec. intervals, successive potentials are not only additive, but grow progressively in amplitude. The growth of the response proceeds smoothly with only slight irregularities, and successive records of this kind show only a minor degree of variation. This is, of course, to be expected,

for this method of recording gives us the averaged response from a large number of end-plates. On the right side we have records obtained with an intracellular electrode from a *single* end-plate, presenting a very different picture. The records show the fluctuating character of the response, there being at first a large proportion of failures with occasional 'single-quantum' responses and then an irregular building up of responses interspersed with occasional failures. In the accompanying table, success-and-failure counts of a large number of such records have been summarized. It will be seen that the proportion of failures progressively diminished during the period of stimulation (84 per cent of failures for the first, about 47 per cent for the tenth and 20 per cent for the fortieth impulse), which corresponds to a progressive increase in the Poisson value of m. If one measures amplitudes of successive end-plate potentials in the left part of the records, it is found that the tenth response is about five times larger, the fortieth response about ten times larger, than the first. A comparison with the results in the table indicates that this increase, or 'facilitation', must be entirely due to a statistical recruitment of quantal units from a large population of units available at each nerve–muscle junction.

RECRUITMENT OF RESPONSE AT A SINGLE JUNCTION
Summary of seven experiments. Intra-cellular recording from end-plates of frog's muscle, treated with high magnesium and low calcium concentration. Repetitive stimulation of nerve, as in records. Second column shows the total number of impulses in the denominator, and the number of end-plate potentials elicited in the numerator

Serial No. of nerve impulses (tetani at 10/sec.)	No. of end-plate responses / No. of nerve impulses	Proportion of failures (= exp (− m))	m	Facilitation factor (m_8/m_1) (mean and S.E.)
N_1	111/710	0·84	0·18	1·0
N_{6-15}	858/1,615	0·47	0·83	4·7 ± 0·45
N_{16-25}	799/1,140	0·3	1·28	7·1 ± 0·66
N_{36-45}	886/1,105	0·2	1·72	9·9 ± 1·25

The basis of the quantal mechanism is unknown: it may be that each unit of discharge starts with the activation of a single 'key molecule', opening a local 'gate' in the nerve membrane and releasing a flood of acetylcholine ions. The activation of such key—or 'carrier'—molecules may result from spontaneous thermal agitation, and the effect of a nerve impulse may be to lower their activation threshold, thus causing a synchronized opening of many local 'gates' and a flooding of the whole end-plate with the transmitter substance. But while there is little doubt about the quantal nature of the end-plate response, and about some of the statistical rules by which it is governed, there is no evidence available at present to support speculations about the details of the quantal mechanism.

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Radio Echoes observed during Auroræ and Terrestrial Magnetic Storms using 35 and 74 Mc./s. Waves Simultaneously

IN an undisturbed and extended ionosphere, the maximum value of the frequency of radio waves which can be reflected by regular refraction processes is determined by the maximum electron density of the layer. The maximum value of the critical frequency at vertical incidence seldom exceeds 15 Mc./s.

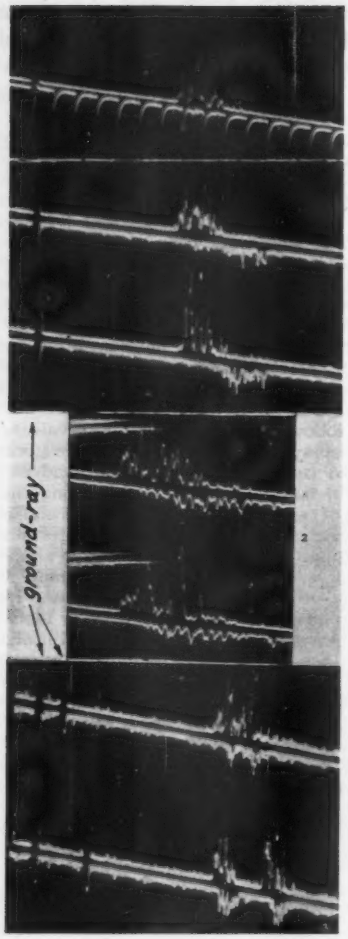
During recent years, considerable attention has been paid to scattering processes of radio waves in the ionosphere. In an inhomogeneous ionosphere it should be possible to get scattered reflexions from 'blobs' or stratifications in the electron densities using waves in the very high frequency band. Scattered reflexions in this have been observed in a number of cases[1]; and in all of them the reflexions have been associated with the appearance in the sky of definite auroral forms.

In the following, the results of observations during auroral displays and terrestrial magnetic storms made at Tromsö (near the auroral zone) and at Kjeller (near Oslo) will be given. The recording equipment consisted of two pulse transmitters on 35 and 74 Mc./s., both having a common pulse-modulator and high-tension supply. The energies and the shape of the two pulses sent out simultaneously could therefore be made identical (peak-power 25 kW. and repetition frequency 50 c./s.). Two geometrically identical six- or three-element yagis, with a half-width of the lobe of 65° directed towards the north, were used as antennæ; the elevation of the beam could be varied. The echoes were displayed on a double-beam cathode-ray tube with common sweep.

The echo records at Tromsö showed that echoes on 35 Mc./s. appeared regularly during auroral displays, and in a number of cases also on 74 Mc./s. A closer study of the echoes led to the conclusion that in the cases under discussion the echoes could not be explained by direct scatter from the ionosphere, but by reflexion of backwards scatter from land or sea via the lower part of the E-layer (the E_s-layer) the ionization of which increases strongly during auroral and terrestrial magnetic storms. Our explanation of the very high frequency echoes observed is therefore in opposition to the common assumption of direct and primary scatter from the auroral forms or inhomogeneities in the ionosphere. The arguments supporting our explanation of the mechanism of reflexion are as follows.

There is no correlation between the ranges of the echoes and the distances to auroræ simultaneously appearing. Even the most brilliant auroral forms appearing at distances from 80 km. (in the zenith) and up to 400–500 km. (low in the north) do not give the slightest traces of echoes appearing when the antennæ are directed against the auroral forms. But at the same time, echoes are observed with ranges of 600–1,800 km. when the antennæ were directed horizontally against the north. It has been assumed[2] that reflexions from an aurora mainly occur when the waves are incident normally to the direction of the earth's magnetic field. In this case we should get no reflexions from the auroræ observed visually in Tromsö. But it is difficult to imagine that this condition is so strictly maintained that the most violent aurora at 80 km. distance does not give the slightest trace of echoes.

In all cases the echoes on 35 Mc./s. showed a noticeably smaller range than the echoes on 74 Mc./s.



Simultaneous echoes on 35 and 74 Mc./s. recorded on a double-beam cathode-ray tube. The upper trace shows 35 and the lower 74 Mc./s., 50 c./s. repetition frequency, recorded on moving film; the distance between the pips represents 100 km. (1) Different reflexion distances for 35 and 74 Mc./s. scatter; (2) lack of correlation between the subsequent sweeps as well as between the 35 and 74 Mc./s. patterns, recorded on an expanded time-scale; (3) double-pulse is used with changing time-separation, and correlation between the echo patterns is obtained when the time separation is of the order of less than 2 millisec.

This difference in range varied and usually amounted to more than 100 km. (see Fig. 1).

The echoes were spread out in time corresponding to a difference in the range from 100 km. and up to several hundreds of kilometres.

Echoes on 35 Mc./s. were considerably stronger than on 74 Mc./s., and echoes on the higher frequency usually appeared during the stronger phases of the terrestrial magnetic storms.

Polarization tests were made on 35 Mc./s. The waves were sent out vertically polarized and received on vertical and horizontal polarized yagis simultaneously through two separate channels. Generally, there was no difference in field-strength of the echoes through the two channels.

With a repetition frequency of 50 c./s., there was no correlation between the echo pattern of subsequent sweeps. In Fig. 2, where the echo patterns are recorded on a fast-moving film, the subsequent echo patterns have changed completely. In this case an increased sweep velocity has been used for analysing the echo pattern.

There is no correlation between the structure of the echo patterns on 35 and 74 Mc./s.

By using double pulses, the distance between the pulses being made variable, it could be shown that a correlation between the echo structures appeared when the time interval between the two pulses was less than about 2 millisec. This corresponds to a ray-path of 300 km., in which case the two echo patterns appeared well separated in time. This is evident from Fig. 3.

There is a difference in character of the echo patterns on 35 and 74 Mc./s. The echoes on 35 Mc./s. exhibited usually a well-defined leading edge with maximum amplitude just after the leading edge. On 74 Mc./s. there was often no leading edge; the echo amplitude increased continuously from zero, and the maximum amplitude was usually considerably displaced towards greater distances.

During one severe terrestrial magnetic storm on November 28, 1952, pulses sent out from Kjeller were received in Tromsö, where they appeared undisturbed, having the same width as the pulses transmitted. During this severe storm the auroral zone had apparently been displaced towards the south and the E_s-layer acted as a mirror-like reflexion surface. The echoes received back at Kjeller, however, showed the usual distortion.

The characteristics of the echoes summarized above cannot be explained by primary scatter from the ionosphere, whereas the assumption of backwards-scatter from land or sea via the lower part of the ionosphere, the E_s-layer, fits in with the characteristics of the echoes described above.

A full account of the observations will be given in *J. Atmo. Terr. Phys.*

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Fractionation of Isotopes by Distillation of some Organic Substances

We have found that the distillation of chloroform, carbon tetrachloride, methyl alcohol and benzene leads, surprisingly enough, in all four cases to an enrichment of carbon-13 in the distillate, whereas the other heavy isotopes, such as chlorine-37 and oxygen-18, are enriched in the still pot.

The distillations were carried out in empty tube columns, consisting of a great number of narrow, unpacked parallel working tubes with individual reflux[1]. All distillations were carried out at 34·6° C. using very high reflux ratios. Samples withdrawn from the head and the bottom of the column were treated in the manner described below to yield gaseous products, such as carbon dioxide and hydrogen chloride, suitable for mass spectrometric analysis. The isotopic abundance ratios were determined by means of a 60° double-collector mass spectrometer (Consolidated–Nier 21–201).

According to the theories of Kuhn[2] and Westhaver[3], the height equivalent to a theoretical plate of empty tube columns may be reduced to a theoretical minimum given by the radius of the tubes (for example, 0·2 cm.), and distillations in which such high separation efficiencies have been very nearly obtained have been reported by Kuhn and Ryffel[4]. The hold-up, and accordingly the time required until equilibrium conditions are obtained, is very small in such columns. The number of effective theoretical plates n of the columns at infinite reflux ratio can be calculated from the length L and the radius r of the tubes, from the average vapour speed $\bar{u}$ and from the diffusion constant D in the vapour according to the relation[2]:

$$n = \frac{4LD}{r^2 \cdot \bar{u}} . \qquad (1)$$

Expressions for n in the case of finite reflux ratios have been derived recently[5].

From the number of theoretical plates n and from the isotopic fractionation, the relative difference in vapour pressure of the isotopic species is calculated according to the following relation derived from the Fenske equation:

$$\frac{p_1 - p_2}{p_2} = \left(\frac{R_B}{R_D}\right)^{1/n} - 1, \qquad (2)$$

where p_1 and p_2 are the vapour pressures at the distillation temperature (34·6° C.) of the pure light and the corresponding pure heavy isotopic molecules respectively, R_B and R_D represent the isotopic abundance ratios in the still pot and distillate, respectively, of the heavy to the light atom under consideration, and n is the number of effective theoretical plates.

The difference in boiling temperatures ΔT of the two isotopic species is approximately obtained from (2) and from the vapour pressure equation using Trouton's rule:

$$\Delta T = T_1 - T_2 = -\frac{T_1^2}{10{\cdot}7\, T_b\, n} \ln \frac{R_B}{R_D}, \qquad (3)$$

where T_1 and T_2 are the absolute boiling temperatures of the pure light and the pure heavy substance respectively at the pressure at which the distillation is performed; T_b is the normal boiling temperature.

If there are several isotopic atoms of the same element in the molecule, for example, chlorine in the case of carbon tetrachloride, the indexes 1 and 2 in equations (2) and (3) can be shown to refer to two isotopic molecules of neighbouring molecular weight, for example, $C^{35}Cl_2{}^{37}Cl_2$ and $C^{35}Cl^{37}Cl_3$ or $C^{35}Cl^{37}Cl_3$ and $C^{37}Cl_4$. This holds in any event, whether exchange of the isotopic atoms between the molecules in the distillation process is possible or not, provided only that the difference in boiling temperatures between all pairs of neighbouring molecules is the same.

Chloroform. Already in 1945 we found that the distillation of chloroform in an empty tube column leads to an enrichment of chlorine-35 in the distillate, the ratio $^{37}Cl/^{35}Cl$ being shifted by amounts up to 12 per cent. The isotope analysis was performed at that time by density measurements, by a spectroscopic method[6], and by using the nuclear reaction $^{37}Cl(n,\gamma)^{38}Cl$[7]. We now find that the agreement with the mass spectrometric ratio determination as performed recently on samples which had been kept from this distillation is satisfactory.

Gaseous hydrogen chloride and carbon dioxide were obtained for mass spectrometric analysis by the reaction of chloroform with potassium hydroxide. The potassium chloride and formate obtained were, after oxidation of the formate to carbonate, treated with acid, liberating hydrogen chloride and carbon dioxide.

From the results of the isotope analysis and from the number of theoretical plates n used in the distillation, the following results were obtained from equations (2) and (3):

Table 1

$n = 610$	Isotopic fractionation of chloroform with respect to: Carbon	Chlorine
R_B/R_D	0·62	1·06
$\frac{p_1 - p_2}{p_2}$	-8×10^{-4}	$+10^{-4}$
$T_1 - T_2$	+0·02° C.	−0·003° C.

Purification of the chloroform for the density determination was carried out as follows. After shaking with concentrated sulphuric acid, the chloroform was distilled off and condensed under vacuum on tetra-salicylide with which, according to Anschütz[8], it forms a very specific addition compound. Upon heating this compound, some low-boiling impurities come off first and are rejected, the pure chloroform being obtained upon further heating. This procedure was repeated several times until no change in density (using the float method) could be observed. To apply the spectroscopic method referred to above, the chlorine must be present in the form of $HgCl_2$, which was obtained from the chloroform by alkaline hydrolysis, precipitation of the chlorine ions as silver chloride and fusing the dried silver chloride precipitate with mercuric sulphate. The mercuric chloride formed according to the reaction $2AgCl + HgSO_4 \rightarrow Ag_2SO_4 + HgCl_2$ is separated from the reaction mixture by repeated sublimation.

Carbon tetrachloride. Attempts to fractionate the chlorine isotopes by high-efficiency distillation of carbon tetrachloride have been reported by Grimm[9] and by Rank and Kargarise[10]. These authors, using the density method of isotopic analysis, did not, however, find any fractionation.

In our case the distillation was carried out in a column with $n = 80$, and the carbon tetrachloride samples were treated for analysis by passing a stream of hydrogen through them and burning the mixture containing some 10 per cent carbon tetrachloride in oxygen. The hydrogen chloride and carbon dioxide thus formed were trapped in an excess of barium hydroxide solution and separated as chloride and carbonate. Pure hydrogen chloride and carbon dioxide were liberated by acid treatment. The following results[1] were obtained.

Table 2

$n = 80$	Isotopic fractionation of carbon tetrachloride with respect to: Carbon	Chlorine
R_B/R_D	0·90	1·003
$\frac{p_1 - p_2}{p_2}$	$-1{\cdot}3 \times 10^{-3}$	$+3 \times 10^{-4}$
$T_1 - T_2$	+0·033° C.	−0·001° C.

The above results indicate that, while there is only a very slight enrichment of chlorine-35 in the distillate, the concentration of carbon-13 is increased considerably. The calculation shows that the resulting effects on the density are of the same order of magnitude but of opposite sign. This would account for the lack of any effect reported in previous studies[9,10].

Methyl alcohol. An enrichment of oxygen-18 in the residue of a methyl alcohol distillation has been reported by Roberts and Urey[11]. In our study, methyl alcohol was distilled in a column with 140 theoretical plates. The samples for investigation were burnt in oxygen of known isotopic composition and the gases thus formed were collected. Water and carbon dioxide were brought to exchange equilibrium at room temperature, and the $^{18}O/^{16}O$ ratio in the methyl alcohol was calculated from that in the carbon dioxide and from that in the oxygen entering and leaving. The results are shown in Table 3. An enrichment of CH_3OD in the still pot was found qualitatively.

Table 3

$n = 140$	Isotopic fractionation of methyl alcohol with respect to : Carbon	Oxygen
R_B/R_D	0·97	1·50
$\frac{p_1 - p_2}{p_2}$	-2×10^{-4}	3×10^{-3}
$T_1 - T_2$	+ 0·0055° C.	− 0·07° C.

Benzene. Pure benzene was distilled in a column with $n = 80$. The samples were burnt in a hydrogen–oxygen flame and the carbon dioxide thus formed was trapped in barium hydroxide solution. The carbonate was decomposed with acid to yield pure carbon dioxide, for which $^{13}C/^{12}C$ analysis led to the following results :

$$R_B/R_D = 0{\cdot}98, \quad \frac{p_1 - p_2}{p_2} = -2{\cdot}5 \times 10^{-4},$$

$$T_1 - T_2 = + 0{\cdot}006° \text{ C.}$$

The results obtained by the distillation of chloroform, carbon tetrachloride and methyl alcohol indicate the possible existence of a general rule stating that, in isotopic molecules having a central atom, the molecular variety containing the heavier isotope of the central atom will exhibit a somewhat higher vapour pressure than the variety containing the lighter isotope as central atom. Results in agreement with this rule have been found recently by Green and Martin[12] in the case of boron trichloride.

We wish to thank Dr. P. Massini for carrying out some of the distillations, Dr. K. Wieland (Zurich) for the spectroscopic isotope analysis of chlorine, and Dr. F. Alder, of the Physics Department, Basel, for the isotope analysis of chlorine by nuclear reaction. This work was supported by grants from the Eidgenössische Volkswirtschaftsstiftung, the Ciba-Stiftung and the Freiwillige akademische Gesellschaft.

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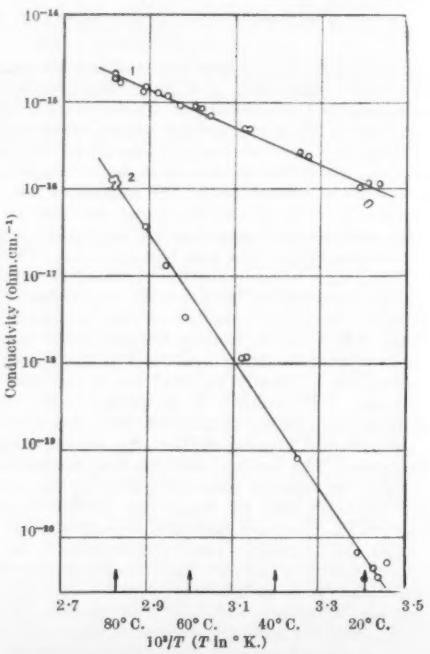
Effect of Temperature on the Conductivity induced in Insulators by X-Rays

Studies of the induced conductivity in insulators due to X-rays[1] are difficult owing to the extremely low values to be measured, and hitherto have been made primarily with condenser chambers[2]. These allow only the after-effect of the radiation to be determined. If measurements of conductivity during exposure are to be made, the apparatus must admit no air gap at any point between the insulator under test and the electrometer, and in addition the volume of insulator irradiated must be as large as possible, so as to give sufficient current for measurement.

These difficulties were overcome in the present tests by using a length of 6 metres of polythene-insulated cable coiled into a flat spiral and connecting the end of the cable, outside the room, to a source of voltage and a D.C. amplifier. The coil was enclosed in a 'Perspex' box through which heated air could be passed to control the temperature. The object was to determine the temperature coefficient both of irradiated and unirradiated material, and hence the energy-levels of conduction bands under the two conditions from the general relationship,

$$\sigma = \sigma_0 \exp(-W/kT).$$

The X-rays were generated at 220 kV. (2·5 mm. copper half-value layer) with a dose-rate of about 8 r./min. The conductivity was measured every minute after commencement of exposure, and the present figures relate to the equilibrium conductivity which is attained after about ten minutes of irradiation. Graph 1 shows the relationship between log (conductivity) and $1/T°$ K. for the range 20–80° C. The straight line confirms the above law for this material. The slope gives $W = 0{\cdot}42$ eV.



(1) Irradiated with X-rays ; (2) unirradiated

The corresponding graph (2) for the unirradiated material is also a straight line, which has a steeper slope, giving $W = 1{\cdot}5$ eV.

It will be observed that in either case the effect of temperature is large. Under irradiation at room temperature, the conductivity increases by 5·6 per cent per deg. C. The corresponding increase for unirradiated material is 19 per cent per deg. C. It is clear from these results that no accurate studies of induced conductivity can be made without very careful temperature control[3]. If such control is applied, however, consistent results are obtained which can be interpreted in terms of energy-level distributions, and the behaviour of the material is not unlike that of crystalline materials[4].

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Degradation of Methionine by Hydrogen Peroxide

I HAVE been searching for an appropriate method of oxidizing methionine from biological materials with hydrogen peroxide in order to be able to detect the amino-acid as its sulphone on paper chromatograms as a discrete spot. During the course of this work, it has been found that the heating of methionine in solutions of hydrogen peroxide leads to the formation of several ninhydrin-reacting substances, some of which are of biological interest as possible intermediates in the metabolism of methionine in animal organisms. In the present communication the procedures employed to effect the degradation of methionine, and the results obtained in a preliminary identification of the substances thus produced, are described.

To study the degradation of methionine in its various stages, 0·05 m*M* aliquots of DL-methionine were added to 0·2–10·0 ml. of hydrogen peroxide solution, the concentration of which was 0·1 m*M* per ml., thus producing mixtures with ratios of methionine to hydrogen peroxide varying from 1 : 0·4 to 1 : 20. These mixtures were sealed in glass tubes and heated in a boiling water-bath for 12 hr. The solutions were then removed from the glass tubes, evaporated to dryness under reduced pressure, and the residues dissolved in 0·5 ml. distilled water. Those reaction mixtures which became strongly acid, as the result of the formation of sulphuric acid, were neutralized with a solution of barium hydroxide, and the resulting precipitate was removed before evaporation. Similar experiments were also carried out starting with methionine sulphoxide and methionine sulphone.

One- and two-dimensional chromatograms were run according to the method described by Williams and Kirby[1]. A phenol – water (80 : 20, v/v) system and a collidine – pyridine – water (150 : 20 : 100, v/v) system were used as developing solvents. For two-dimensional chromatography, 1–10 µl. portions of the solutions of reaction products prepared as described above were used.

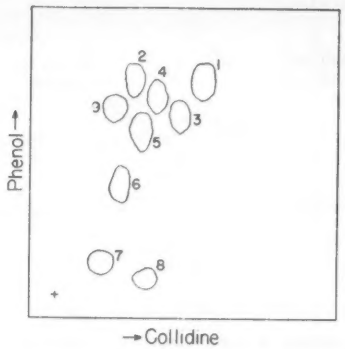


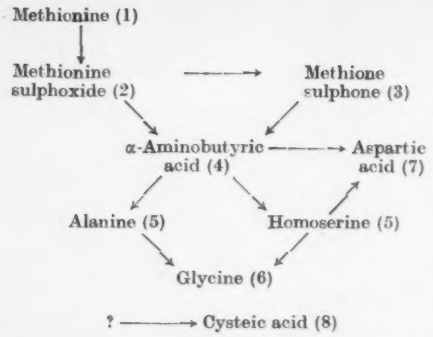
Diagram of two-dimensional chromatogram of ninhydrin-reacting substances derived from methionine by oxidation with hydrogen peroxide. 1, methionine; 2, methionine sulphoxide; 3, methionine sulphone; 4, α-aminobutyric acid; 5, alanine or homoserine, or both; 6, glycine; 7, aspartic acid; 8, cysteic acid; 9, unknown

The accompanying diagram is a composite one of the spots appearing on the two-dimensional chromatograms, and it shows all the ninhydrin-reacting substances derived from methionine by oxidation with hydrogen peroxide. All these spots on the paper chromatograms showed the typical ninhydrin reaction of amino-acids, and none of them survived the distinctive test for α-amino-acids reported by Crumpler and Dent[2]. Identification of these substances was carried out only by means of paper chromatography.

Neither of the solvents used in this study, nor their combination in the two-dimensional technique, could separate alanine and homoserine completely. In another experiment, solutions of alanine and hydrogen peroxide were heated in the presence of sulphuric acid. The chromatographic analysis of the product of this reaction could support the interpretation that glycine was formed from alanine. Since, as mentioned above, sulphuric acid is formed when methionine is heated in a solution of hydrogen peroxide, it might be suggested that spot 5 is alanine, and glycine (spot 6) is derived from alanine. However, it is possible that spot 5 is homoserine, because homoserine was found to give rise to glycine and aspartic acid under the same conditions. It was also found that under the same conditions α-aminobutyric acid can yield glycine, aspartic acid and spot 5. Therefore, spot 5 can be interpreted as being either alanine or homoserine; or it may represent both amino-acids.

All the spots shown in the diagram, except that of methionine, were observed in the reaction mixtures when the experiment began with methionine sulphoxide. When methionine sulphone was used instead, spots 4 and 5 could not be detected; and, of course, spots corresponding to methionine and methionine sulphoxide were absent in this case. The reason for the absence of spots 4 and 5 may be that methionine sulphone is very stable under the conditions of this experiment; α-aminobutyric acid and the substance represented by spot 5, which are less stable in comparison to methionine sulphone, are rapidly converted to other oxidation products.

Cysteic acid might be produced by a reaction between sulphuric acid and a 3-carbon moiety, though no proof of this has been obtained. The nature of spot 9 is unknown.



Possible pathway of degradation of methionine by hydrogen peroxide

A possible pathway for the degradation of methionine under the experimental conditions employed in this work is shown in the diagram. That α-aminobutyric acid can be derived from methionine through its sulphoxide, and very possibly also through its sulphone, is most interesting.

Thanks are due to Drs. T. Minoshima and H. Nakamura for their interest in this work.

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Crystalline Trypsin

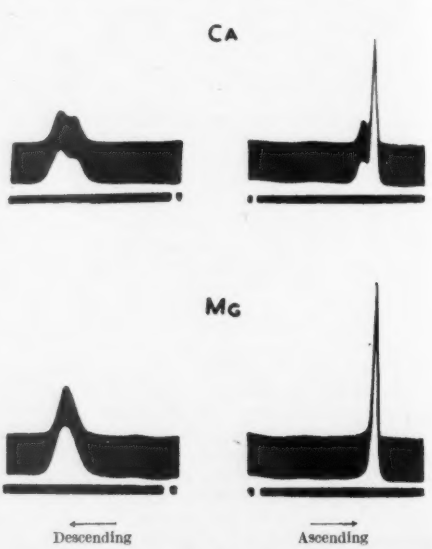
Investigations carried out during the past two years have revealed the existence of a complex interaction between trypsin and certain specific divalent ions, particularly calcium ions. These relations manifest themselves in various ways and have been studied in arbitrarily differentiated *p*H-stability zones of trypsin.

In the region of its optimum proteolytic activity, between *p*H 7 and 9, calcium and manganese ions were the only ones in a comprehensive list of ions tested which stabilize trypsin solutions[1,2]. By means of electrophoretic analyses performed in this *p*H region, it could be demonstrated that the calcium effect is due to a diminishing of the rate of self-digestion, and it was concluded that calcium causes a shift in the equilibrium existing between the native and denatured forms of the enzyme towards the former. This work also resulted in a redetermination of the isoelectric point of the enzyme, which lies in the neighbourhood of *p*H 10·8, and was amplified by a partial determination of the amino-acid composition[1]. The same ions, as well as cadmium and cobalt ions, were found to augment slightly the activity of the enzyme[3], while an investigation over the whole *p*H range has shown that the higher activity can be ascribed to the increased concentration of the active form of the enzyme[4]. On the other hand, calcium has shown itself to be without specific protective effect in inactivation of the enzyme brought about by ionizing radiation[5].

The maximum stability zone of the enzyme is at about *p*H 2·3. Ultracentrifugal sedimentation patterns are characteristic of a homogeneous protein having a sedimentation constant $s_{20,w}$ of 2·5 *S* [6] or 2·4 *S* [7]. On prolonged standing at the acid side of this *p*H, some faster sedimenting components appear as a result of the aggregations of the slowly denaturing enzyme which is not complicated by proteolysis. The sedimentation behaviour at *p*H 8 is quite similar to that observed at acid *p*H with the exception that, on prolonged standing, some slower sedimenting products of the self-digestion appear. The presence of either of these breakdown products or of the aggregated enzyme in acid solutions does not influence the sedimentation-rate of the remaining unaltered trypsin[7].

It is between the above two extreme *p*H regions that a number of other significant manifestations of the effect of calcium can be observed. It was reported that the sedimentation constant increases in this range, the maximum aggregation being at about *p*H 5 [8]. Our investigations resulted in the observation that this aggregation is strongly dependent on temperature, the sedimentation constant decreasing to about a normal value at 30° C. The presence of 0·05 *M* calcium chloride completely prevents this aggregation[7]. More direct evidence of an interaction between calcium and trypsin in this *p*H range was obtained by the study of the dissociation curves of trypsin. Calcium ions, in contrast to magnesium ions, give rise to a shift in the titration curves of the enzyme in the regions of the dissociation of carboxylic groups towards more acid *p*H values. The formation of the complex thus demonstrated causes the lowering of the dissociation constants of the carboxylic groups[4].

It was therefore to be expected that the decrease in net charge of the enzyme, due to the formation of the complex with calcium, could be evidenced by electrophoretic analysis. The characteristic patterns



Characteristic electrophoretic patterns of trypsin in presence or absence of calcium ions. Ca, buffer 0·04 *M* sodium acetate, 0·033 *M* calcium chloride, *p*H 5; Mg, buffer 0·04 *M* sodium acetate, 0·033 *M* magnesium chloride, *p*H 5

of trypsin at *p*H 5, in 0·04 *M* acetate buffer, in the presence of 0·033 *M* magnesium or calcium chloride, all other conditions being equal, are shown in the accompanying diagram. It can readily be seen that, in the absence of calcium, trypsin presents an electrophoretic pattern characteristic of a homogeneous compound, the presence of calcium ions causing the separation of the moving boundary into two well-defined peaks. Of the two boundaries, the larger one moves with a mobility characteristic of trypsin in the absence of calcium, and the smaller boundary moves at a slightly slower rate. At a lower concentration of calcium ions, the appearance of the secondary peak is not so well defined; but further increase in the calcium ion concentration does not change the electrophoretic patterns. It is characteristic that identical patterns are also observed in the presence of manganese as well as cadmium ions which have already been mentioned as increasing the activity of the enzyme[3]. Cobalt, magnesium and barium ions, listed in order of decreasing effect, also increase the activity of trypsin, but to a lesser degree than calcium, manganese or cadmium ions, which are equivalent in their action. Under our experimental conditions, neither of the first three ions causes the characteristic change in the electrophoretic pattern; together with all other ions tested, they give rise to electrophoretically homogeneous patterns of trypsin. Nevertheless, there is no doubt that the two effects are due to the same cause.

After a prolonged electrophoretic separation, it was possible to obtain small samples of the faster and slower components. In four independent analyses, the tryptic activity of both components was found to be proportional to the concentration of the protein as determined by ultra-violet absorption at 280 mμ. Crystalline trypsin was also digested at *p*H 8 in the presence and absence of calcium, and aliquot samples were analysed electrophoretically at 24-hr. intervals, the electrophoretic analyses having been carried out in the presence of calcium under the conditions already mentioned. It was thus possible to determine the rate of digestion of both components in the presence or absence of calcium. In both instances it was found that the ratio of the areas of the two components did not change in the course of the self-digestion, although the overall rate of digestion was considerably diminished by the presence of calcium. It appears, therefore, that crystalline trypsin is electrophoretically heterogeneous, containing two components both of which possess a similar tryptic activity and rate of self-digestion and both of which are subject to protection by calcium ions. An indication of this heterogeneity has already been reported[1].

Another example of an electrophoretically heterogeneous protein in which all components have similar biological activity was found in ovomucoid[8], the antitryptic factor of egg-white. The aggregation observed in the absence of calcium by ultracentrifugal analysis is viewed as resulting from a reversible interaction of the two components. As a consequence, only one peak appears in electrophoretic analysis, moving with the weighted average of the mobilities of the two components. Calcium, combining with the carboxyl groups, prevents this aggregation, resulting in a normal sedimentation behaviour and appearance of the two electrophoretic components.

We acknowledge the assistance of T. Langen and L. Terminiello in this work, which is being carried out under the ægis of the U.S. Atomic Energy Commission.

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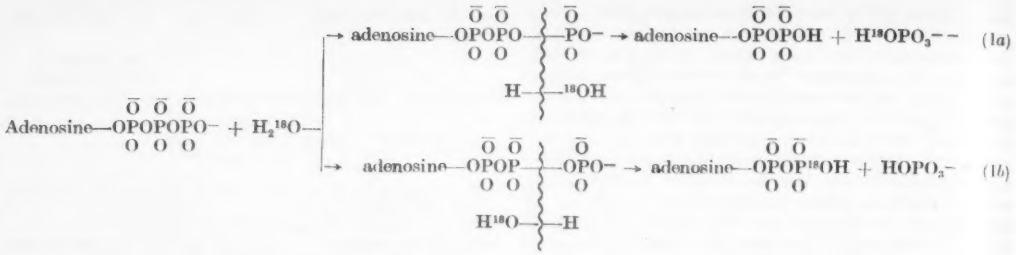
Mechanism of Hydrolysis of Adenosine Triphosphate catalysed by Lobster Muscle

In previous publications[1] evidence has been presented for the occurrence of displacement mechanisms in a wide variety of enzymatic reactions to which those of adenosine triphosphate are closely analogous. Assuming that the adenosine triphosphate reactions proceed by the same mechanisms, it can be deduced from the nature of the products that the adenosine triphosphate can undergo nucleophilic attack at any of its three phosphorus atoms. As examples, the Lohmann reaction with creatine[2] must involve attack at the terminal phosphorus atom, the coenzyme A reaction of Lipmann *et al.*[3] must involve attack at the middle phosphorus atom and the Kornberg reaction with nicotinamide mononucleotide[4] must involve attack at the innermost phosphorus atom. If the adenosine triphosphate is hydrolysed by an adenosine triphosphatase in ordinary water to adenosine diphosphate and inorganic phosphate, the pathway is not obvious, since attack at either the terminal phosphorus atom or the middle phosphorus atom would give the same products. This ambiguity can be avoided, however, by using $H_2{}^{18}O$, in which case the alternatives are clearly distinguishable (cf. reaction 1). The study of the mechanism of adenosine triphosphate hydrolysis in muscle was therefore performed in a medium of $H_2{}^{18}O$ and the products were analysed for their content of oxygen-18.

Lobster muscle strips (25 gm.) were thoroughly washed with potassium chloride solution and then incubated with $H_2{}^{18}O$ (100 c.c., 1·3 atom per cent excess) for 1 hr. until equilibration between the water of the medium and that of the muscle strips had occurred. Solid adenosine triphosphate (2·55 m*M*) was then added, and the solution was stirred for 30 min. until 77 per cent of the adenosine triphosphate had been hydrolysed to the diphosphate and inorganic phosphate. After removing the muscle strips, the phosphate compounds were precipitated as the barium salts and separated on ion exchange columns following the procedure of Cohn and Carter[5]. Operations subsequent to the enzymatic hydrolysis were performed in the cold under conditions which were shown to prevent appreciable decomposition of the labile compounds. To ensure purity of the separated products, only the middle fractions of each well-isolated peak were used in the subsequent analyses.



Determination of oxygen-18 showed that the terminal group of the adenosine triphosphate, the terminal group of the diphosphate, and the inorganic phosphate contained 0·0514, 0·00513 and 0·815 atom per cent excess per atom of oxygen, respectively.

Control experiments were performed in which (*a*) the medium contained ordinary water, and inorganic phosphate labelled with phosphorus-32 was added with the adenosine triphosphate, and (*b*) the medium contained $H_2{}^{18}O$ but only inorganic phosphate was added to the solution. In experiment (*a*), the hydrolysis was 64 per cent complete, and the adenosine tri- and di-phosphate and the muscle strips contained 0·11, 0·016 and 4·3 per cent of the total counts added, respectively. In experiment (*b*) the inorganic phosphate had 0·026 atom per cent excess.

From the small oxygen-18 content of the adenosine diphosphate, it is clear that the mechanism of hydrolysis catalysed by the muscle phosphatase(s) involves a nucleophilic displacement on the terminal phosphorus atom. The oxygen-18 present in the unhydrolysed adenosine triphosphate results predominantly from exchange with, or synthesis from, the intracellular inorganic phosphate, since the quantity of labelled element determined agrees with that calculated from the phosphorus-32 control experiment if appropriate corrections for diffusion-rates and extent of hydrolysis are made. The oxygen-18 content in the adenosine diphosphate is likewise correlated with its phosphorus-32 content in the control experiment.

The oxygen-18 content of the inorganic phosphate per atom of oxygen would be one-quarter that of the medium from the direct hydrolysis of adenosine triphosphate (cf. reaction 1 *a*). The fact that it is considerably higher than this shows that the muscle preparation catalyses a net transfer of oxygen between inorganic phosphate and water. This is further confirmed by the observed exchange in control experiment (*b*). The total exchange is less in the latter case than in the hydrolysis experiment presumably because the inorganic phosphate is released inside the cell in the hydrolysis experiment, whereas in control (*b*) the inorganic phosphate is initially extracellular. From the measured metabolic-rates in the lobster muscle preparation it can be calculated that the increased oxygen-18 content of the inorganic phosphate is caused only in minor part by the recycling of inorganic phosphate through adenosine triphosphate, and must be due in large part to a more direct exchange reaction. A somewhat similar exchange which does not go through high-energy phosphate has been observed in mitochondrial preparations by M. Cohn[6]. Since it has been shown that the exchange with inorganic phosphate can be catalysed by a single enzyme[1b], it is conceivable that the reaction in the muscle may also be caused by an individual enzyme which catalyses a nucleophilic attack on phosphorus.

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Possible Role of Proteolytic Enzymes in Protein Synthesis

Bergmann[1] has proposed that proteolytic enzymes mediate in the biological synthesis of proteins from amino-acids. The 400–4,000[2] or more[3] calories per mole required for peptide bond formation from *free* amino-acids can, however, be provided only when synthesis is coupled with an energy-yielding reaction[4]. To accommodate this energy requirement, Brenner, Hanes, Fruton and co-workers[4a] have demonstrated that a variety of proteolytic enzymes catalyse a reaction of esters, amides, or peptides (including the naturally occurring peptide, glutathione) with amines or amino-acids in which new amides or peptides are formed. The enzymes show their usual specificity; that is, they synthesize only those peptide bonds that they also hydrolyse. The energy requirement is met by the initial ester, amide or peptide linkage which is split, for there is presumably very little difference in energy between the bond destroyed and that formed. These workers have shown beyond doubt that some or perhaps most proteolytic enzymes can catalyse polypeptide synthesis from amino-acids, providing there is an independent method of 'energizing' the amino-acid (ester, amide, peptide, etc.). From there it is possible to speculate that in a similar way these proteolytic enzymes play a part in normal protein synthesis.

As a test of this hypothesis, Hendler and Greenberg[5] have recently studied the metabolism of labelled γ-glutamyl-glycine; but they found that this particular compound is not significantly involved in any of several living systems that incorporate amino-acids into proteins. The evidence presented here also does

not appear to be consistent with the hypothesis outlined above.

We have described techniques for measuring the rate of incorporation of various radioactive amino-acids such as glycine and alanine into the protein of tissue slices, and have outlined reasons for believing that this is closely related to biological protein synthesis[6]. Using these techniques, we have incubated α-aminobutyric acid-1-^{14}C with rat liver slices. When the protein is isolated and the amino-acids separated by chromatography[7], we find that the labelled aminobutyric acid has been incorporated into the protein to only a very slight extent, if at all. The ratio of alanine incorporation to aminobutyric acid incorporation is at least one hundred and fifty to one, and may be much higher when improved chromatographic techniques are used. We find, however, that these two amino-acids are oxidized to the α-keto-acids and to carbon-14 dioxide at a similar rate by the liver slices, and that there is, at the end of the experiment, about the same intracellular level of aminobutyric acid as of alanine. Clearly, we have shown that aminobutyric acid is as actively carried into the cell as alanine, and as effectively utilized in some reactions, but that those enzymes which are responsible for protein synthesis in the living cell are sufficiently specific to reject aminobutyric acid, the next higher homologue of alanine and the next lower homologue of valine.

Such specificity is striking and is in agreement with the concept, which has gained so much support from the recent work of Sanger and Tuppy[8] on the structure of insulin, that a protein is a specific compound with a perfectly definite amino-acid sequence. One may ask whether every protein of the cell has such a definite structure.

Are the proteolytic enzymes of the cell sufficiently specific to reject α-aminobutyric acid 150 to 1 with respect to alanine? It is inherent in the theory of catalysis that the catalyst should not affect the equilibrium of a reaction; hence that it must accelerate the forward and reverse reactions equally. The catalytic activity of a given enzyme in synthesizing aminobutyrylglycine can be roughly estimated by measuring the rate of hydrolysis of the dipeptide. To be precise, the rate of hydrolysis corresponds to the rate of synthesis from two free amino-acids, the rate of ethanolysis corresponds to synthesis from the ethyl ester and one free amino-acid, etc.

In all cases that have been reported, aminobutyric acid-peptides are split at rates comparable with the corresponding alanyl-peptides. However, the enzymes used were extracellular. Smith and Polglase[9] found that α-aminobutyric acid amide was split by leucine amino-peptidase from intestinal mucosa at a rate between alanyl- and leucyl-amide. We have measured the rates of hydrolysis of alanyl-, aminobutyryl-, and leucyl-glycine by the proteolytic enzymes of freshly homogenized rat liver, that is, precisely the tissue which rejects aminobutyric acid for protein synthesis. The accompanying results show that aminobutyrylglycine is split by these intracellular enzymes at about the same rate as alanylglycine under these conditions.

While this may be taken as evidence against the participation of proteolytic enzymes in normal protein synthesis, it is not conclusive. A wide range of aminobutyric acid peptides should be tested. It is also possible that the great degree of specificity of protein synthesis is found in the enzymes acting on the larger peptides. We feel, however, that unless an enzyme system does discriminate against aminobutyric acid or an aminobutyric acid peptide, the system being studied should not be considered as part of the mechanism of biological synthesis of protein.

HYDROLYSIS OF PEPTIDES

Substrate	Concentration	% Hydrolysis
DL-Alanylglycine	0·16 *M*	41
	0·08 *M*	85
DL-α-Aminobutyrylglycine	0·17 *M*	37
	0·09 *M*	63
DL-Leucylglycine	0·12 *M*	10
	0·06 *M*	16

1 gm. of fresh rat liver homogenized in 10 c.c. 0·1 *M* phosphate buffer, *p*H 8·2; suspension centrifuged, supernatant diluted 1 : 40 with same buffer, and used as source of enzyme. Incubation mixture: 1 c.c. of enzyme solution, 1 c.c. of peptide solution, 0·01 c.c. of toluene. Temp. 37°.

Incubation time, 6 hr. Hydrolysis determined by ninhydrin method (ref. 10). Per cent calculated for L-isomer only; hydrolysis of D-isomer considered to be negligible.

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A Disulphide Interchange Reaction

IN experiments designed to determine the position of the —S—S— bonds in insulin, cystine peptides were separated from a partial acid hydrolysate, and their structures determined after oxidation to the corresponding cysteic acid peptides. It was found that many more cystine peptides were present than could be accounted for by any one unique structure for the insulin molecule, and it seemed likely that a transfer reaction of the type:

$$R^1\text{—S—S—}R^2 + R^3\text{—S—S—}R^4 \rightleftharpoons R^1\text{—S—S—}R^3 + R^2\text{—S—S—}R^4$$

had taken place during the hydrolytic treatment, leading to a random rearrangement of the —S—S— bonds. That such a reaction can take place was

illustrated by the following model experiment, in which *mono*-2 : 4-dinitrophenyl-cystine is formed from a mixture of cystine and *bis*-2 : 4-dinitrophenyl-cystine.

1 mgm. *bis*-2 : 4-dinitrophenyl-cystine and 10 mgm. cystine were incubated with 2 ml. of 12 *N* hydrochloric acid. After 24 hr. at 37°, 5 ml. water and 10 ml. ether were added and the mixture shaken. Nearly all the yellow colour was found in the aqueous layer, indicating the presence of *mono*-2 : 4-dinitrophenyl-cystine. In a control experiment without cystine, all the colour which was due to *bis*-compound was in the ether layer. The reaction-rate is rapid in strongly acid or in neutral solution and is minimal in dilute acid (about 0·1 *N* hydrochloric acid). This probably explains the fact that insulin is inactivated more readily by heating in neutral than in dilute acid solution[1], if the rearrangement of the —S—S— bridges is assumed to cause inactivation.

The mechanism of the reaction is not clear at present and is under investigation. It may involve the intermediate formation of an —SH compound by reduction or hydrolysis, in which case the actual rearrangement would be brought about by the reaction :

$$-R^1\text{—SH} + R^2\text{—S—S—}R^3 \rightleftharpoons R^2\text{—SH} + R^1\text{—S—S—}R^3.$$

In this case the R^2—SH formed would be available to react with a further disulphide, so that only a catalytic amount of an —SH compound could bring about considerable rearrangement[2].

I wish to thank Dr. G. Weber for some valuable advice in connexion with this work.

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Structural Features of Antitumorigenic Corticoids

The antifibromatogenic potency of deoxycorticosterone—prevention of œstrogen-induced abdominal fibroids—diminishes through the substitution O=C_{11} (Kendall's compound *A*) and especially through OH--C_{17} (Reichstein's compound *S*)[1]. The antifibromatogenic potency of cortisone, which differs from deoxycorticosterone by both these substitutions, is also strikingly diminished ; there were fibroids even with as much as 1,000 μgm. of cortisone acetate per day. But, on the other hand, there apparently was some antifibromatogenic activity of compound *F*, or 17-hydroxy-corticosterone (OH--C_{17} and OH—C_{11}); we had thus to raise the question of a 'protective' action of OH—C_{11} against OH--C_{17}. However, in view of the variations of the fibrous tumoral effect met with in similar experiments, and especially in view of the small number of experiments performed with compound *F*, the conclusion as to the supposed 'protective' action of OH—C_{11} against OH--C_{17} remained doubtful[1]. In the meantime, we have been able to settle this question in what seems to be a definite manner, thanks to the kindness of Messrs. Merck and Co., who put at our disposal the necessary quantities of compound *F* acetate.

Ten animals (castrated female guinea pigs) were used in the experiment, which lasted 91–92 days. An average of 81 μgm. of œstradiol per day was absorbed from subcutaneously implanted tablets ; 268–447 μgm. (average 350) of compound *F* acetate was absorbed per day from two tablets (a new implantation six weeks after the first one). There were fibroids in nine out of ten animals ; average fibrotumoral effect, 5·2 ; average weight of uterus, 4·6 gm. The quantities of compound *F* were indeed smaller than in some animals of the former series, in which there apparently was prevention ; but there is the fact that fibroids were present in the new series, even with quantities as large as 350–447 μgm. of compound *F* acetate per day. It is thus evident that OH—C_{11} does not afford 'protection' against OH--C_{17}, by which antifibromatogenic potency is so greatly diminished (compound *S*).

Although we must drop our original concept of 'protection' by OH—C_{11} against OH--C_{17} with reference to antifibromatogenic corticoids, it is very remarkable that the same concept seems to be valid with reference to the inhibition of the growth of the chick embryo, as evidenced by certain findings of Stock[3]. The effective growth-inhibiting dose of deoxycorticosterone is 250 μgm. ; that of compound *S* (OH--C_{17}) is as high as 5,000 μgm. ; but the effective dose of compound *F* (OH--C_{17} and OH—C_{11}) is only 20 μgm.

Attention may also be directed to a comparative discussion of the structural features of antifibromatogenic and antilymphomatogenic corticoids[3].

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Multi-spots in Paper Chromatograms

During investigations on the synthesis of nucleotides in this laboratory, extensive use has been made of the paper chromatography of phosphorus-containing compounds. In the early experiments it was observed that in a descending pyridine – ethyl acetate – water system, disodium hydrogen phosphate gave two clear spots of approximately equal intensity with R_F 0·17 and 0·55 on spraying with molybdate reagent[1]. Identical spots were obtained with sodium or potassium mono- or di-hydrogen phosphates, whereas ammonium phosphate and free orthophosphoric acid gave only the faster-running spot. Trisodium phosphate showed largely the slower spot with some trailing. (These R_F values are quoted to give an indication of the positions of the spots. The temperature was not strictly controlled.) Other experiments showed the effect was not due to complexes with pyridine as the same double-spot phenomenon occurred in a butanol – water system. By buffering the phosphates with acid and alkali, it was found that the number of spots depended on the *p*H of the solution in which the phosphate was applied to the paper. Potassium dihydrogen phos-

phate below *p*H 3 gave only the faster running spot; between *p*H 3 and *p*H 9, both spots at R_F 0·17 and 0·55 were in evidence, but by *p*H 10 (caustic soda added) only the slower spot appeared. Above *p*H 12 only a spot at R_F 0·05 was obtained with a horse-shoe appearance (compare Paterson and Reincke[2]).

Further experiments were carried out using phosphoric acid containing phosphorus-32. When used in tracer amounts, it was found that the counts from the radioactive phosphorus agreed in position with the colours from the spraying. As an indication of the discreteness of the spots, it was found that a count of 6,000 a minute at the site of the spots fell between them to less than 100. When, however, phosphoric acid having a specific activity of 1 mC./ml. was diluted with water and adjusted in *p*H with suitable acetate buffers, it was found that in this case, with the quantity of phosphate infinitesimal compared to the usual concentration of 0·04 *M*, there were no 'double spots'. Instead, at *p*H 2·5 there was one site of counts at R_F 0·55, whereas at both *p*H 4 and *p*H 5·5 counts were only at R_F 0·17. As before, at *p*H 14 the phosphate concentration was at R_F 0·05.

It is considered from these results that it is possible that the spot at R_F 0·55 is given by the $H_2PO_4^-$ ion, that at R_F 0·17 by the HPO_4^{--} ion and that at R_F 0·05 by the PO_4^{---} ion.

The mechanism of the separation of these spots is difficult to visualize. If the equilibrium $H_2PO_4^- \rightleftharpoons HPO_4^{--} + H^+$ were disturbed by the separation of the faster-running $H_2PO_4^-$, then the equilibrium should readjust itself and cause extensive trailing. One explanation is that the time of proton transfer in this equilibrium is slow. An experiment was devised that could to some extent check this. $H_3{}^{32}PO_4$ was mixed with $Na_2H^{31}PO_4$ and the mixture put on a chromatogram. If the $H_3{}^{32}PO_4$ (which existed as $H_2{}^{32}PO_4^-$) did not exchange with the $H^{31}PO_4^{--}$, then no counts should be found at the slower-running spot. When this experiment was carried out, counts were found at both sites. This means that the time required for equilibrium must be shorter than that required for the spots to separate on paper.

There have been other reports of double spots in paper chromatographic experiments[1,2]; but in these cases it is possible that they were due to interference of un-ionized compounds with inorganic ions or to impurities in the paper. All the experiments described above were conducted on No. 1 Whatman paper which had been washed with 2 *N* acetic acid, and it is not considered possible for this multiplicity to be caused by contamination.

Evidence that the *p*H of the solution in which the specimen is applied to the paper affects the R_F of the resultant spot has been amply demonstrated in the case of the amino-acids[3], and it has been suggested that the separation of lysine into different ionic species may be due to association with phenol in the developing solvent[4].

Whatever the cause, this double-spot phenomenon does mean that, where polyvalent ions are encountered, it is possible that multi-spots may be obtained.

Two examples encountered subsequent to the work with inorganic orthophosphate may serve as an indication of the care necessary in the interpretation of experiments that have been followed by paper chromatography. Pure 2′ : 3′-*iso*propylidene adenosine-5′-dibenzyl phosphate[5] was hydrogenated in an effort to obtain 2′ : 3′-*iso*propylidene adenosine-5′-phosphate. The final product could not be crystallized but showed on chromatography in an ascending butanol – acetic acid solvent two spots of R_F 0·56 and 0·64. On acid treatment to remove the acetone group, only adenylic acid remained, and since it was not a case of one of these spots being either adenylic acid or a monobenzyl ester of it or the acetone derivative, it is possible that they are both derived from the divalent 2′ : 3′-*iso*propylidene adenosine-5′-phosphate. The other example was that of adenosine diphosphate run in a descending butanol – acetic acid solvent giving one spot when in low concentration, and this splitting into two spots when the concentration was increased.

I would like to thank Prof. A. R. Todd and Dr. G. W. Kenner for much advice during these investigations.

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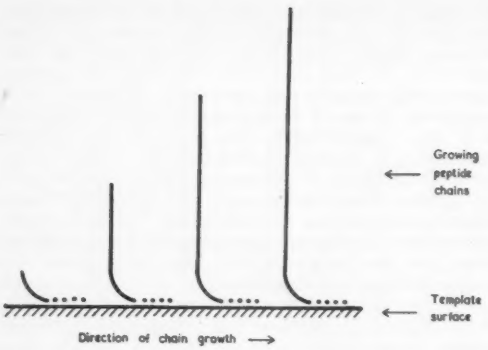
The Template Theory and the Role of Transpeptidation in Protein Biosynthesis

The synthesis of protein occurs without detectable evidence of free peptide intermediates. This fact, and the specificity of proteins, have been explained by the so-called 'template theory', in which it is assumed that the amino-acids are laid down in their correct order on a template (? consisting of nucleic acid) with subsequent bond formation and separation from the template[1]. Recent work has shown that transpeptidation occurs with peptides in artificial systems[2], and evidence has been sought for the participation of transpeptidation in protein synthesis. In these experiments protein synthesis has been brought about in the presence of isotopically labelled amino-acid. The resultant protein is degraded, the appropriate amino-acid isolated from two different parts of the chain and the specific activities compared. It is assumed that if the template theory is correct, all amino-acids must be laid down on the template effectively simultaneously, so that differences in activity of the same amino-acid residue in different parts of the chain are evidence for transpeptidation[3]. We wish to show that this assumption is not necessarily justifiable.

Energy considerations make it most unlikely that a complete protein molecule is formed on a template surface and afterwards separates as a whole from the surface. It is much more probable that amino-acids become attached to the surface of the template, and that as the amino-acid residues link together, the growing peptide chain 'peels off' behind the zone of formation of peptide bonds, as has been postulated in the recent theory of Dounce[4]. In such a case the protein does not finally separate from the surface until it is complete (so that no intermediate steps are observed); but only a small region is attached to the template at any time. Moreover, after a 'wave' of biosynthesis has passed down the template surface, the latter can be reactivated, further replacement by



amino-acids can occur, and a further 'wave' of biosynthesis may pass along. Many peptide chains at different stages of growth may thus be attached to the template at the same time, as is suggested in the diagram.

If a template were to carry simultaneously twenty growing protein molecules in different stages of development, the actual time of biosynthesis of each molecule would be twenty times the apparent time per molecule. Thus the time of biosynthesis of a protein may be much longer than is generally supposed. In the biosynthetic experiments, the amino-acids are drawn from a pool with which the labelled amino-acid may or may not have become equilibrated. In any normal biological system, the specific activity of the pool changes with time, and to show that differential degrees of labelling of the same amino-acid residue in different parts of a protein chain are due to transpeptidation, it must be shown that the difference is too great to be accounted for by changes with time in the activity of the pool. Conclusions are therefore not valid without evidence of the time of biosynthesis of a single molecule of the particular protein being investigated. No such evidence appears to be available, so that transpeptidation cannot yet be said to have been demonstrated in protein biosynthesis.

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Quantitative Estimation of the Total Solids in Fresh Whole Milk by Oxidimetry

Since the major organic constituents of milk, with the possible exception of the fat, carry readily oxidizable groups, it should be possible to measure their amount by oxidimetry. Although the fat itself may not be readily oxidizable, it may possibly be measured indirectly by means of the substances associated with it in the fat phase and which are probably present in proportion to the amount of fat. Thus it would appear reasonable to believe that an oxidimetric method could be devised for measuring the total solids of milk. Such a test could be carried out much more rapidly and simply than by the methods usually employed.

After several trials using ceric sulphate in *N* sulphuric acid and ferrous-*o*-phenanthroline as oxidant and indicator respectively, the following method was tentatively adopted as a means of testing the theory.

The milk was secured from the weigh-tank and 10 ml. was diluted to 100 ml. with distilled water and well mixed. 10 ml. of the diluted milk was transferred to a casserole containing 20 ml. of distilled water, two drops of ferrous-*o*-phenanthroline were added and the mixture titrated against 0·01 *N* ceric sulphate in *N* sulphuric acid until the orange colour was discharged. The titration was continued after the lapse of one minute, and the total number of millilitres of ceric sulphate used was taken as the titre value of the milk. (It was found that titrating at a constant rate yielded closer agreement between duplicates.)

Thirty-one samples of herd milk representing milk from five different breeds of cows were tested by this method, and the results compared with the value for total solids obtained with the A.O.A.C. gravimetric method ("Methods of Analysis", A.O.A.C., 7th edit., 1950).

The results yielded a coefficient of correlation between titre values and total solids values of $r = 0{\cdot}912$ with a standard error of estimate of $\pm\ 0{\cdot}238$ per cent total solids. It is noteworthy that the error between duplicate titrations was approximately $\pm\ 0{\cdot}05$ ml., causing a final error of $\pm\ 0{\cdot}22$ per cent in the total solids, which is in good agreement with the standard error of estimate.

While the above method in its present form may not serve as a practical means for measuring the total solids in milk, it does justify the view that such measurements may be done by oxidimetry, and should serve as a starting point in the search for a rapid and accurate method.

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A New Linkage in Tobacco

In about seven genetic linkages so far found in *Nicotiana* species, only one concerns *tabacum* and another *rustica*. The rest of the five linkages were discovered in interspecific crosses involving *N. tabacum*, *N. langsdorffii* and *N. sanderæ*[1]. Kelaney[2] found a linkage between a gene *Br* for broad-constricted leaf with the gene *Pk* for carmine-pink flowers with a 7·5 per cent crossing-over. Boortzev[3] mentions linkage of 4·35 per cent between seed colour and compact habit in *N. rustica*. Clausen and Cameron[4] have isolated twenty-four monosomics of tobacco and were able to locate cytologically eighteen genes for sixteen characters in nine chromosomes by crossing the monosomics with a standard tobacco type. In six of the chromosomes identified, more than one gene has been found, but the authors do not mention the position of genes and distances between them.

We present here a new case of linkage between a gene for petiolate condition and absence of auricle of leaf found in a cross made during 1949–50 between Lanka and Yellow-Special varieties of *N. tabacum*.

F_2	$Pt\ Au_0$	$Pt\ au_0$	$pt\ Au_0$	$pt\ au_0$	Total	χ^2	P
Obs.	16	2	2	5	25		
Exp. 9 : 3 : 3 : 1	14·06	4·69	4·69	1·56	25	10·953	0·01
Exp. 16·6 per cent cross-over	16·84	1·91	1·91	4·34	25	0·1508	0·90–0·95
Exp. 19·988 per cent cross-over	16·5012	2·2482	2·2482	4·002	24·99	0·4630	0·80
Back-cross							
Obs.	16	5	4	18	43		
Exp. 1 : 1 : 1 : 1	10·75	10·75	10·75	10·75	43	12·5263	< 0·01
Exp. 20·93 per cent cross-over	17·00	4·50	4·50	17·00	43	0·2288	0·80–0·90
Exp. 19·988 per cent cross-over	17·2026	4·2974	4·2974	17·2026	43	0·2402	0·80–0·90

Lanka is an indigenous variety grown exclusively in the islands formed by the Godavari River ; it has a petiolate leaf with no auricle, but very slight growth of tissue in its place. Yellow-Special is a flue-cured type originally obtained from America, and has sessile leaves with large auricles which extend down the stem. The F_1 was petiolate and developed only a thin fringe at the leaf base, which was slightly more prominent than in Lanka, indicating that petiolate condition and absence of auricle are dominant characters. The F_2 generation consisted of eighteen petiolate and seven sessile plants. For the other character also there happened to be eighteen non-auricled and seven auricled plants. Thus both the characters showed monogenic inheritance. The back-cross ($F_1 \times$ Yellow-Special) confirmed the F_2 behaviour. The gene pairs are designated *Pt*–*pt* and Au_0–au_0.

When the F_2 and back-cross data were considered for joint segregation of the two characters, in both cases there was significant disagreement between the observed and the expected frequencies on the basis of independent assortment of the two genes. Determination of linkage intensities gave 16·6 per cent cross-over for F_2 and 20·93 per cent cross-over for back-cross. A pooled estimate[5] from the two populations gave 19·988 ± 5·49 per cent cross-over. The relevant data are presented in the accompanying table.

From these results it can be concluded that the gene *Pt*, for petiolate condition of leaf, is linked at about 20 morgans with the dominant gene Au_0 for absence of auricle.

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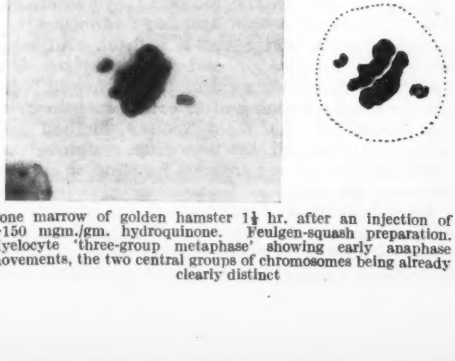
Production of 'Three-Group Metaphases' in the Bone-Marrow of the Golden Hamster

A few years ago, a new type of chemically produced abnormality of mitosis, henceforth termed 'three-group metaphase', appearing shortly after an injection of hydroquinone, in the intestinal germinative cells of the mouse, was reported in *Nature*[1]. Later, the rat also proved itself to be a convenient material, while the guinea pig, the chick and chick fibroblast cultures were not responsive as regards this effect[2].

With the opportunity of using new techniques and material, the same phenomenon has been observed not only in the intestine but also in the bone marrow of the golden hamster in the first six hours following an intraperitoneal injection of hydroquinone, in doses varying from 0·150 mgm. to 0·200 mgm./gm. These mitoses, characterized by an apparently normally formed metaphase plate and by aberrant chromatic bodies localized at the poles of the spindle, appear with high incidence in the cells of the granular series, whereas the erythroblast divisions remain apparently unaffected. Almost at the same time, pycnotic nuclei become more and more numerous and the number of white cell mitoses gradually decreases, so that after twenty-four hours mature polynuclears are relatively more abundant.

With this possibility of further investigation into the mechanisms of this peculiar lesion, it has now become evident that the hypothesis of chromosome breakage put forward in our first publication cannot be maintained for mammals, even though it has been demonstrated to hold true in plant cells[3]. In fact, the polar Feulgen-positive bodies can be ascertained to represent well-formed and defined chromosomes, with their longitudinal fissuring very often apparent. Our further suggestion[4], that these aberrant chromosomes were retained in the centrosome region and did not undergo their pre-metaphase migration, gains strong support from the evidence of morphological features of some of the altered metaphases. Indeed, this explanation is in accordance with the finding of numerous asymmetrical figures—metaphase plate and one polar group—which cannot be attributed to an early anaphasic migration of the smaller chromosomes after their normal division.

Furthermore, seeking for intermediary figures, a few later stages have been discovered, which, obviously independent of chromosome fragmentation, strongly enhance the hypothesis of the possible completion of these mitoses. They consist of early anaphases with the metaphase plate clearly split in two. At this stage, the aberrant chromosomes are still visible



Bone marrow of golden hamster 1½ hr. after an injection of 0·150 mgm./gm. hydroquinone. Feulgen-squash preparation. Myelocyte 'three-group metaphase' showing early anaphase movements, the two central groups of chromosomes being already clearly distinct

at the poles of the spindle (see photograph). Later, they can no longer be identified as they probably become hidden among the normal and rapidly migrating chromosomes. After six hours, when the destructive action is most evident, some of the 'three-group metaphases' have been observed to participate in the pycnotic effect. The three separate groups sometimes undergo chromatic condensation, giving rise to another peculiar image which could be termed 'three-group pycnosis'. While they are not visible twenty-four hours after the injection, there is still no evidence that all the 'three-group metaphases' are destroyed in this manner.

More detailed observations on the action of hydroquinone and related substances on the bone-marrow and other tissues of the mouse, the rat and the rabbit, and on the cellular changes causing this new type of pathological mitosis, will be published shortly elsewhere.

These experiments were started during a short stay at the Chester Beatty Institute, London, and I wish to express my thanks especially to Dr. P. C. Koller.

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[4] Parmentier, R., and Dustin, P., *Caryologia*, **4**, 98 (1951).

A New Method in Staining Bacteria on Microscope Slides

A new method of providing dyes for some of the commoner staining procedures has been developed and tested. A small volume of the required dye solution is prepared according to the appropriate formula. The fluid is placed in a large dish, and rounds of No. 4 Whatman filter paper are soaked in it. After a few seconds the paper is removed by means of flat forceps and hung over a glass rod to dry. The dye-paper is then cut into suitable 'chips'—papers 1½ in. long by ¾ in. wide are found to give good results. One round of 11 cm. diameter paper will provide a useful number of dye-papers which can be stapled together in the form of a booklet, with a plain paper cover. The dye-papers do not stain dry fingers and they can be made by unskilled labour in any laboratory.

For use in simple staining, a drop of distilled water is placed on the fixed film and a dye-paper placed on it; two more drops of water will give enough concentration of dye to stain the bacteria in the operative time. The paper is then washed off and the film dried.

Papers soaked in the following dye solutions are now in use for simple staining: aqueous crystal violet, aqueous and carbolic fuchsin, and aqueous safranin. Aqueous or carbolic methylene blue is used for demonstrating granular diphtheroid bacteria, and for counterstaining after carbol fuchsin in staining spores by the Ziehl–Neelsen method (carbol fuchsin is followed by a sodium sulphite paper). Carbol fuchsin papers are used for staining capsulated cells and flagella[1].

The advantages of the dye-paper method, with the dyes so far tested, include: (1) elimination of fluid stains in bottles; (2) economy of dye; (3) economy of storage space; (4) non-spoilage (as by rubber, oxidation, etc.); (5) ease of preparation; (6) negligible cost.

P. H. H. Gray
Department of Bacteriology,
Macdonald College,
Que., Canada. Nov. 5.

[1] Gray, P. H. H., *J. Bact.*, **12**, 273 (1926); **45**, 301 (1943).

Elimination of Inconclusive Results in the Treponemal Immobilization Test

Working with Nichols's pathogenic strain in the treponemal immobilization test, it is a common experience[1] that some sera constantly yield inconclusive results and, further, that from time to time a whole series of results must be discarded, because one or another of the controls shows poor survival of the treponemes.

When the test is performed in an atmosphere of 95 per cent nitrogen and 5 per cent carbon dioxide 'contaminated' with about 0·2 per cent oxygen, inconclusive results are relatively often obtained. Even when all oxygen is removed by slow passage of the air through a heated tube of quartz filled with copper chips, there still remain a few sera giving inconclusive results. Consequently, it is necessary to remove all the oxygen; but even then, satisfactory survival of the treponemes is not always obtained.

It was thought that great reducing power in the survival medium might be of importance. Hence, the treponemal immobilization test was performed with a medium containing four times the concentration of sodium thioglycollate ('Difco') prescribed by Nelson.

Preliminary experiments with increased amounts of sodium thioglycollate showed that it was possible to get just as satisfactory results in the test with the above-mentioned oxygen-contaminated atmosphere as with a 'normal' concentration of sodium thioglycollate in an oxygen-free mixture. When the test was performed with four times the normal concentration of sodium thioglycollate in an oxygen-free mixture, it was to be expected that none or only very few sera would give inconclusive results. As a matter of fact, no inconclusive results have been observed since this modification has been employed (150 sera examined).

Hence it is assumed that substances in the testicular extract from rabbits now and then are able to raise the oxidation reduction balance (redox potential) of the medium to such a level that it is incompatible with satisfactory survival of the spirochætes. However, the same might happen in sera giving inconclusive results in experiments in which other sera give satisfactory results. So far no bad influence of the increased amount of sodium thioglycollate has been observed.

Further experiments are in progress, and it is intended to measure *Eh*, *rH* and *p*H through the different phases of the treponemal immobilization test. Special electrodes and beakers, manufactured by Radiometer, Copenhagen, have made this possible.

Hans Aage Nielsen
Serodiagnostic Department,
State Serum Institute, Copenhagen.
June 13, 1952.

[1] Durel, P., Sausse, A., and Borel, L. J. (personal communication). Nelson, R. A., *Amer. J. Hyg.*, **48**, 120 (1948). Nelson, R. A., Zheutlin, H. E. C., Diesendruck, J. A., and Austin, P. G. M., *Amer. J. Syph., Gonor. and Ven. Dis.*, **34**, 101 (1950). Turner, T. (personal communication).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, June 8

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE, PHILOSOPHY OF SCIENCE GROUP (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. E. H. Hutten: "Models in Physics".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.15 p.m.—Mr. Ian Stephens: "Two Principalities in Central Asia".

Tuesday, June 9

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Madame S. Filitti Wurmser (Paris): "Étude quantitative de l'isohémagglutination humaine".*

Wednesday, June 10

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers.

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Madame S. Filitti Wurmser: "Les isoagglutinines anti-B de divers génotypes".*

Thursday, June 11

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Sir Ronald Fisher, F.R.S.: "Population Genetics" (Croonian Lecture).

MINERALOGICAL SOCIETY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers.

ROYAL AERONAUTICAL SOCIETY (at the Institution of Mechanical Engineers, Storey's Gate, St. James's Park, London, S.W.1), at 6 p.m.—Sir Hubert Walker: "Some Problems in the Development of Air Transport in West Africa" (Ninth British Commonwealth and Empire Lecture).

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

VICE-PRINCIPAL (with honours degree in mechanical or aeronautical engineering, and considerable teaching and industrial or research experience)—The Principal, Royal Aircraft Establishment Technical College, Farnborough, Hants (June 13).

ASSISTANT LECTURER IN PHYSICS (with good honours degree)—The Secretary, St. Mary's Hospital Medical School, Paddington, London, W.2 (June 15).

LECTURER IN AGRICULTURAL ZOOLOGY (preferably with special interest in ecology), a LECTURER IN PHYSIOLOGY (preferably with special interest in the physiology of the special senses and neurophysiology), an ASSISTANT IN ZOOLOGY, and an ASSISTANT IN PHYSIOLOGY—The Secretary of University Court, The University, Glasgow (June 15).

ASSISTANT LECTURER IN GEOLOGY (with honours degree in geology, and preferably some research experience in stratigraphy and palæontology)—The Secretary, University College, Gower Street, London, W.C.1 (June 15).

RESEARCH ASSISTANT (with degree in chemistry) IN THE DEPARTMENT OF CHEMISTRY AND BIOLOGY, for polarography and other electrochemical techniques, general microchemistry and design of apparatus, etc.—The Secretary, Norwood Technical College, Knight's Hill, London, S.E.27 (June 15).

ENTOMOLOGIST at the Royal Army Medical College, Millbank—The Civil Service Commission, Scientific Branch, Trinidad House, Old Burlington Street, London, W.1, quoting S.4214/53 (**June** 18).

LECTURER IN THE DEPARTMENT OF PHYSIOLOGY, BIOCHEMISTRY AND PHARMACOLOGY, to teach medical organic chemistry—The Registrar, King's College, Strand, London, W.C.2 (June 18).

SENIOR SCIENTIFIC OFFICERS as RESEARCH ENGINEERS in the Royal Naval Scientific Service, for post (*a*) structural, (*b*) mechanical, (*c*) mechanical—hydraulics, in the Naval Construction Department, Bath—The Civil Service Commission, Scientific Branch, Trinidad House, Old Burlington Street, London, W.1, quoting S.4212/53 (June 18).

ASSISTANT EXPERIMENTAL OFFICERS (2) at the Forest Products Research Laboratory, Princes Risborough, for work on the strength of timber in its various uses—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting C.98/53A (June 19).

DEMONSTRATOR IN PHYSIOLOGY—The Secretary, London Hospital Medical College, Turner Street, London, E.1 (June 20).

GEOLOGIST (with honours degree in geology, and preferably with experience in geological mapping and economic geology)—The Secretary, Southern Rhodesia Government, Rhodesia House, 429 Strand, London, W.C.2 (June 20).

SENIOR PRINCIPAL SCIENTIFIC OFFICER as Head of the Admiralty Petroleum Laboratory, Brentford—The Civil Service Commission, Scientific Branch, Trinidad House, Old Burlington Street, London, W.1, quoting S.4210/53 (June 25).

SENIOR RESEARCH OFFICER or RESEARCH OFFICER (with a degree in veterinary science and postgraduate training or experience in bacteriology or serology) at the Animal Health Laboratory, Parkville, Victoria, to carry out researches on approved aspects of bovine contagious pleuropneumonia, and to be responsible for the production of vaccine—The Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting 201/74 (June 27).

JUNIOR LECTURERS (2) IN CHEMISTRY (one to teach Advanced Physical Chemistry and the other to teach Elementary Inorganic Chemistry and to assist in the supervision of First Year Laboratory Classes) at Auckland University College—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (July 15).

SENIOR LECTURER IN CIVIL ENGINEERING at the University of Queensland—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (July 31).

APPLIED PHYSICISTS and RESEARCH ENGINEERS (senior and junior posts) in the Sheffield laboratories, for research in industrial metal working processes such as rolling and forging—The Personnel Officer, British Iron and Steel Research Association, 11 Park Lane, London, W.1, quoting "Metal Working".

ASSISTANT BIOCHEMIST (basic grade) (with university degree or equivalent) to work under general direction of group pathologist and senior biochemist—The Secretary, Preston Royal Infirmary, Preston.

EXPERIMENTAL OFFICERS and ASSISTANT EXPERIMENTAL OFFICERS (ENGINEERS or PHYSICISTS with a strong interest or research experience in electronics or telecommunications, line and radio) in the Royal Naval Scientific Service, in the London area and Gloucestershire—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.136/53A.

LECTURER (male) (with honours degree in agricultural science specializing in agricultural zoology, or honours degree in zoology) IN THE BIOLOGY DEPARTMENT, to give lectures in zoology as applied to agriculture, etc.—Dr. N. T. Gill, Harper Adams Agricultural College, Newport, Shropshire.

PHYSICIST (with first- or second-class honours degree or equivalent in physics) in the Metallurgy Department, Royal Aircraft Establishment, Farnborough—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.136/53A.

PLANT PATHOLOGIST (with honours degree in science and postgraduate research and practical experience in plant disease control) for investigational and experimental work in connexion with plant diseases, more particularly diseases of bananas, in the Cameroons Development Corporation Estates, West Africa—The Rubber and Mining Agencies, Ltd., 52 Leadenhall Street, London, E.C.3.

VICE-CHANCELLOR—The Registrar, University of Otago, P.O. Box 56, Dunedin, New Zealand; or the Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1.

REPORTS and other PUBLICATIONS

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Sir John Cass College. Report, Session 1951–52. Pp. 20. (London: Sir John Cass College, 1953.) [204

Air Ministry: Meteorological Office. Meteorological Reports No. 12: Aviation Meteorology of the Route Marseilles—Rome—Athens—Cairo. (M.O. 535g.) Pp. ii+68. (London: H.M. Stationery Office, 1953.) 2*s.* 6*d.* net. [204

Department of Scientific and Industrial Research: Radio Research. Special Report No. 23: Characteristics of the Ionosphere Observed in Great Britain, 1930–1946. Pp. vi+16. (London: H.M. Stationery Office, 1953.) 1*s.* 6*d.* net. [204

British Museum (Natural History). Guide for the Identification and Reporting of Stranded Whales, Dolphins, Porpoises and Turtles on the British Coasts. By F. C. Fraser and H. W. Parker. Second edition. Pp. viii+42. 2*s.* Instructions for Collectors, No. 3: Reptiles, Amphibians and Fishes. Sixth edition. Pp. 28. 9*d.* (London: British Museum (Natural History), 1953.) [214

Report of the Proceedings of the 1952 Conference of the Universities of Great Britain and Northern Ireland, convened by the Committee of Vice-Chancellors and Principals, and held in the William Beveridge Hall, University of London, Senate House, on Friday and Saturday, December 12th and 13th, 1952. Pp. 103. (London: Association of Universities of the British Commonwealth, 1953.) [214

British Non-Ferrous Metals Research Association. Thirty-third Annual Report, 1953. Pp. 59. (London: British Non-Ferrous Metals Research Association, 1953.) [214

Fire Protection Association. Technical Booklet No. 11: A Comparison of the Extinguishing Effects of Chlorobromomethane Methyl Iodide and Carbon Tetrachloride. By E. H. Coleman. Pp. 12. Technical Booklet No. 12: The Surface Spread of Flame on Surfaces treated with Nitrocellulose Lacquers. By R. W. Pickard. Pp. 12. Technical Booklet No. 13: The Heating of Panels by Flue Pipes. By D. I. Lawson, L. L. Fox and C. T. Webster. Pp. 20. (London: Fire Protection Association, 1952.) [214

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Wool Industries Research Association. Report of the Director of Research for 1952–53. (Publication No. 196.) Pp. 27. (Leeds: Wool Industries Research Association, 1953.) [214

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Commonwealth Relations Office. The Colombo Plan: Technical Co-operation Scheme. Report for 1952 by the Council for Technical Co-operation, Colombo, February 1953. Pp. 16. (London: H.M. Stationery Office, 1953.) 6*d.* net. [284

Society of Chemical Industry: Chemical Engineering Group. Proceedings, Vol. 33, 1951. Pp. viii+82. (London: Society of Chemical Industry, 1953.) 42s. [304

Cambridge University Educational Film Council. Sixth Report, 1953. Pp. 8. (Cambridge: Cambridge University Educational Film Council, 1953.) [304

Textile Institute. Annual Report, Balance Sheet and Accounts for 1952. Pp. 20. (Manchester: Textile Institute, 1953.) [304

University of Leeds. Report to the Worshipful Company of Clothworkers of the City of London of the Advisory Committee on the Departments of Textile Industries and Colour Chemistry and Dyeing during the Session 1950–51. Pp. 41. Report to the Worshipful Company of Clothworkers of the City of London of the Advisory Committee on the Departments of Textile Industries and Colour Chemistry and Dyeing for the Session 1951–52. Pp. 38. (Leeds: The University, 1951–1952.) [304

Science Museum. Navigation Today: a Special Exhibition at the Science Museum, London, from April–September 1953. By D. Chilton. Pp. v+21+7 plates. (London: H.M. Stationery Office, 1953.) 1s. 6d. net. [304

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Philosophical Transactions of the Royal Society of London. Series A: Mathematical and Physical Sciences. No. 904, Vol. 245: A Transformation of the Hodograph Equation and the Determination of certain Fluid Motions. By T. M. Cherry. Pp. 583–626. (London: Cambridge University Press, 1953.) 9s. 6d. [304

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Royal Institute of Chemistry. Lectures, Monographs and Reports, 1953, No. 2: Plant Growth Substances. By Dr. R. L. Wain. Pp. ii+16. (London: Royal Institute of Chemistry, 1953.) 5s. net. [304

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Canada: Department of Mines and Technical Surveys, Mines Branch. Technical Paper No. 1: The Determination of Thorium in Ores by the Column Method. By R. J. Guest. Pp. vi+24. 25 cents. Technical Paper No. 2: The Constitution of Bone China, Part 1, High Temperature Phase Equilibrium Studies in the System Tricalcium Phosphate-Alumina-Silica. By P. D. S. St. Pierre. Pp. v+107. 50 cents. (Ottawa: Department of Mines and Technical Surveys, 1953.) [204

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Scientific Council for Africa South of the Sahara. Publication No. 3: Directory of Scientific and Technical Libraries in Africa South of the Sahara. Pp. 61. (Kikuyu: Scientific Council for Africa South of the Sahara, 1953.) 2s. 6d. [304

Survey of Egypt. Survey Department Paper No. 52: The Artesian Water of Egypt. By G. W. Murray. Pp. iv+20. (Giza: Survey of Egypt, 1952.) 4·00 mills. [304

Annual Reports for 1941–51 of the Pathological Division of the Rubber Research Institute of Malaya. Pp. 50+34+34. (Kuala Lumpur: Rubber Research Institute of Malaya, 1953.) [304

Notas de Física. No. 8: On the Spread of the Soft Component of Cosmic Radiation. By G. Molière. Pp. 5. No. 9: Non-Relativistic Equation for Charged Particles with Spin 3/2. By J. Tiomno. Pp. 9. (Rio de Janeiro: Centra Brasileiro de Pesquisas Físicas, 1952.) [45

Annalen van de Sterrewacht te Leiden. Deel 20, Tiende en elfde Stuk: Improved Elements of 84 Southern Cepheids, by C. J. Van Houten; Discussion of 43 Variable Stars in a Region around CPD − 31° 5547, by P. Th. Oosterhoff and Miss J. A. Horikx. Pp. 273–318. (Leiden: Sterrewacht, 1952.) [45

Mémoires de la Société de Physique et d'Histoire Naturelle de Genève. Vol. 42, Fascicule 3: Distribution de la radioactivité en Suisse. Par Roger Payot et Adrien Jaquerod. Pp. 253–320. (Genève: Georg et Cie., 1953.) 10 francs. [45

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